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See also SAUNDERS Announcement on Page 3

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THE MAKING OF AN OPHTHALMOLOGIST

CHAIRMAN'S ADDRESS

CONRAD BERENS, M.D.
NEW YORK

In guiding the medical student who desires to practice ophthalmology or in advising the young ophthalmologist, stress should be laid on education, ethics, research and the importance of attending medical meetings.

Older ophthalmologists can be of great assistance to young men by merely setting a good example in clinical practice, by offering their assistance in training and by imparting the results of their experience. The question of the adequate training of the ophthalmologist seems to be especially important at this time because of the disorganization of educational opportunities and depletion of teaching staffs due to the war. Therefore this subject has been chosen for presentation. Certainly there has been excellent precedent in the Transactions of the Section [1] for this type of discussion.

EDUCATION

The medical curriculum of the ophthalmologist should include comprehensive courses in higher mathematics, biology, chemistry, physics, modern languages and, if possible, elementary courses in embryology, comparative anatomy, physiology, bacteriology and physiologic chemistry. In medical school the student should be permitted to elect certain subjects which will aid him in ophthalmology. For example, he should be encouraged to devote more attention to clinical ophthalmology than to clinical obstetrics. He should have a keen interest in the fields closely related to ophthalmology and have the privilege of continuation studies in fundamental work, particularly anatomy, embryology, pathology and immunology in relation to ophthalmology. This statement should not be construed as suggesting that the ophthalmologist's training should not be as broad as possible in general medicine but merely that some time should be available for elective studies.

After graduating from medical school there is a question of a general hospital internship. Some ophthalmologists consider this period of training a waste of time. However, the stimulation and broadening influence derived from close association with and observation of the work of the great leaders in medicine and surgery makes a general internship the most important part of a man's medical training. A hospital where the young physician can obtain stimulation from outstanding clinicians and teachers should be his first choice. Although the American Board of Ophthalmology and most of the states require only one year of training in a general hospital, I believe that from eighteen months to two years is not too much time for the ophthalmologist to devote to this part of his training and that the major part should be devoted to internal medicine. It is regrettable that our medical students today are to have only nine months of general hospital experience and that the Army has been unable to arrange for some degree of selection of the medical school by the applicant.

The next step is usually a residency of two or three years in an eye hospital or eye department of a well equipped general hospital. During this period of training the ophthalmologist acquires by apprenticeship proficiency in the technics of operations and methods of treatment and learns to use his hands under the guidance of experienced surgeons. The clinical judgment acquired by experience aided by apprenticeship under a good clinician may be even more important than surgical technic. One of the best and most valuable parts of an eye resident's hospital training is that received from his senior resident; the young ophthalmologist should make rounds with him and observe and write his notes. In doing this he will profit greatly, as will hospital records. Unfortunately in peacetime there are not enough residencies in the country for all young ophthalmologists to receive this type of training. Therefore other means of training must be provided, for example, working in a clinic or in an office with an ophthalmologist who is a good clinician and who keeps adequate records.

If possible the student should have a course in the basic sciences related to ophthalmology before he enters active hospital work. He should work toward an advanced degree and should be stimulated to undertake a specific research problem and prepare a thesis preferably while he is having basic science training. My observation leads me to believe that men so trained make better residents and benefit more from their special hospital training. If it is not feasible to obtain a course in the basic sciences, one should attend lectures and demonstrations by members of the hospital staff, attend meetings of ophthalmologic sections and enroll in the Home Study Course sponsored by the American Academy of Ophthalmology and Otolaryngology under the direction of Dr. Harry S. Gradle.

The education of war veterans presents a special problem. Many of our young men have been called into the military services in the middle of their hospital or basic science training. Even before the President's message to Congress concerning the postwar education of veterans for from one to three years, ophthalmolo-

Read before the Section on Ophthalmology at the Ninety-Fourth Annual Session of the American Medical Association, Chicago, June 14, 1944.

1. Knapp, A.: Importance to the Practicing Ophthalmologist of Contributing to Literature, Tr. Sect. Ophth., A. M. A., 1926, p. 17. Todd, F. C.: Research in Ophthalmology and the Training of Ophthalmologists, ibid., 1914, p. 17. Holloway, T. B.: The Correlation of University Research, ibid., 1930, p. 17. Greenwood.[3] Snell.[2] Heckel.[2]

gists, guided by suggestions made by Dr. Gradle, have been planning for the teaching of ophthalmology to physicians released from our armed services. The instruction will be given with little, if any, cost to our confrères who have sacrificed so much for those of us who remained at home. The undertaking of the entire expense by the government may or may not be desirable and should be carefully studied.

ETHICS

While ethics may be taught by lectures, the conduct of older ophthalmologists provides the greater stimulus. Several of our chairmen have ably presented this problem in their chairman's addresses.[2] The county medical societies are influential in maintaining and raising ethical standards, especially when the higher type of physicians take an active part in the work of the society. The boards of censors of these societies act on complaints from other medical practitioners and the public concerning unethical actions of member physicians.

Young ophthalmologists as well as any physician should appreciate the importance of never detracting from the standing or the work of his confrères. A man's own position is never helped when he attempts to make himself important by belittling his colleagues. Another grave mistake is to speak disparagingly of large fees obtained by other men. If the fees are large but commensurate with ability to pay and the service rendered is of high quality and honest, colleagues should be delighted. To my knowledge no honest physician ever became rich through the practice of medicine, and physicians in private practice give more of their time to charity in one way or another than they can physically or financially afford.

ETHICS AND OPTOMETRY

One of the most important problems in ethics from the standpoint of public service and public health is that of optometry. Those who believe that optometrists should be taught certain subjects and that there should be closer cooperation between ophthalmology and optometry are apparently in conflict not only with the Oath of Hippocrates, "I will impart a knowledge of the art to my own sons and those of my teachers, and to disciples bound by a stipulation and oath, according to the law of medicine, but to none other," but also with certain resolutions passed by this section in 1936, which were reaffirmed in 1942. I believe this part of the Hippocratic Oath should be reconsidered by ophthalmologists in the light of conditions existing in 1944 and that the entire matter should be returned to the individual state and county societies.

Some members of the section have said that insufficient consideration has been given to optometry and that the only place where these problems have been discussed has been in the brief executive meetings of the section. These statements have been made without knowledge of the facts, for the Section on Ophthalmology appointed a committee on optometry as far back as 1913, designating Dr. William C. Posey as chairman. This question was thoroughly and ably discussed by Hiram Woods in 1913 and by Walter B. Lancaster in 1928 in their chairman's addresses. Having served as secretary of the American Committee on Optics and Visual Physiology and as a director of the National Society for the Prevention of Blindness, I have gradually accepted the conclusion that lack of cooperation between ophthalmologists and all others concerned with vision and eye health is the most serious unsolved problem in the prevention of blindness today.

Those who have been closely associated in the study of this problem believe, almost to a man, that optometrists should be taught by those best qualified to teach subjects which would aid in preventing blindness. A recent vote taken by the American Ophthalmological Society and by this section indicates a similar opinion among a large and growing group of ophthalmologists. I believe that a careful unbiased study of the reasons why so many men are now in favor of cooperation, by those who hold opposite views, would lead to a change of opinion in many cases.

The armed forces have used optometrists under the close supervision of ophthalmologists, and in the great majority of instances of which I have personal knowledge the arrangements have been mutually satisfactory to the ophthalmologists and to the optometrists. Because of this, ophthalmologists have asked whether a similar arrangement would not be satisfactory in private practice, as this association has also proved useful in some of the nation's municipal and private hospitals. This is one problem a special committee of the American Medical Association might well study to the mutual benefit of all concerned.

In spite of the existence of the 1942 optometry resolution, we should cooperate in preventing the introduction of bills in our state legislative bodies and the publication of articles in scientific or lay journals which fan the flame of a feud. The feud between the two groups concerned with eye care not only lessens the faith of the public in all types of eye service but also shakes public confidence in medical care in general, because few laymen can define the terms optometrist, ophthalmologist and optician.

I urge each young ophthalmologist and every member of this section to study this problem from the aspect of public health, service to the public and the prevention of blindness, without prejudice engendered by personalities or by financial considerations.

FEE SPLITTING AND PARTICIPATION IN THE SALE OF GLASSES

Several of my predecessors who have discussed similar subjects [3] have had nothing to say on fee splitting for operations, drugs, x-ray examinations and hospitalization. However, I believe that this practice is so little indulged in by ophthalmologists in spite of one or two recent isolated examples that it may be dismissed. All ophthalmologists should strive to eliminate these practices by their example and by aiding American medicine in the fight against this degrading and dangerous evil practice.

Profits from the sale of glasses is another matter which cannot be too heartily condemned if money is received for no service rendered or no financial risk assumed. Undoubtedly in many communities ophthalmologists must dispense their own glasses, and if the lenses were sold without profit these ophthalmologists might be in unfair competition with the opticians and other persons associated with eye care, who could not afford to dispense glasses at cost. The ophthalmologist who dispenses his own glasses usually would prefer to find a reliable optician or encourage one to settle in his

2. Lancaster, W. B.: The Optometry Problem, Tr. Sect. Ophth., A. M. A., 1928, p. 97. Snell, A.: Some Principles of Medical Ethics Applied to the Practice of Ophthalmology, ibid., 1941, p. 17. Heckel, E. B.: The Ethics of Ophthalmology, ibid., 1929, p. 17.

3. Greenwood, A.: The Organization and Activities of the Ophthalmic Service in the American Expeditionary Forces, Tr. Sect. Ophth., A. M. A., 1919, p. 87. Snell.[2] Heckel.[2]

community. Thus he could free himself from conducting a business which, if it continues for any length of time, frequently becomes a financial necessity.

It is my conviction that all those associated with eye care, who participate to any great extent in the sale of glasses, even though they perform a service in dispensing lenses and thus are able to charge low fees for their consultations, are in unfair competition with those who do not participate. Even when ophthalmologists or optometrists dispense glasses without profit, they are still in unfair competition with those who do not dispense their own lenses.

If when beginning practice the young nonparticipating ophthalmologist makes his fees low in order to permit him to compete with ophthalmologists and optometrists who do participate in the sale of glasses, it will later be hard for him to raise his charges. However, to start his practice with adequate fees may be so difficult as not to be practical. There is no question that it is preferable from the standpoint of the public and medicine to give honest, real medical service and charge for it than only to seem to give low cost service. Some of the plans for prepayment of medical service stress low fees for eye examination but neglect to mention profit from glasses. This tendency to cheapen the apparent cost of medical service by hidden profits should be carefully watched, studied, discouraged and prevented.

There is no doubt that the great majority of medical men, especially those who are willing to submit to regulation by organized American medicine, are ethical and wish to have nothing to do with merchandising. There are many sides to this complicated problem and many points of view which must be respected until we know every angle of the situation which has caused ophthalmologists to take a certain stand.

If all ophthalmologists and optometrists could and would free themselves from the personal dispensing of glasses, ethical standards would be raised.

This is too complex and important a subject to be discussed fully in the time at my disposal and requires study by a special committee with adequate funds to make a comprehensive investigation.

RESEARCH AND STUDY

Fortunately for the advancement of science, there are many young ophthalmologists who are interested in the broader concept of medicine. They should be associated with a clinic where they may be broadened by contact with other physicians. They should be interested in teaching and research and should stimulate others in investigative work. Some of the best and most important research may be done in the clinic.[4]

Office records should be complete so that they may be valuable for research. The young ophthalmologist should be constantly thinking of how he can improve his technic of examination and his instruments. He should attempt to make treatment less empirical. This is a form of research any one can do. Qualified men or those who can work under the supervision of competent ophthalmologists should endeavor to contribute to the knowledge of the many unsolved problems in ophthalmology, for example the etiology of chronic uveitis, cataract and glaucoma. Several foundations may be approached, if the problem to be studied is well presented and seems to offer the possibility of advancing science. The John and Mary R. Markle Foundation, Snyder Ophthalmic Foundation, the Ophthalmological Foundation, the Josiah Macy Jr. Foundation and several others have contributed funds for research in ophthalmology.

Ophthalmologists should contribute to the literature and keep well informed concerning the writings and the technics of other surgeons and read current medical journals, not only the ophthalmic publications but also those in fields related to ophthalmology, e. g. embryology, physiology, bacteriology, immunology, pathology and, of course, psychiatry, medicine, general surgery and neurology.

ATTENDANCE AT MEDICAL MEETINGS AND PARTICIPATION IN LOCAL OPHTHALMIC ACTIVITIES

The young ophthalmologist should attend local eye meetings and contribute to them. In addition to attending local meetings of ophthalmologists he should become a member of the Association for Research in Ophthalmology. This association has been developed with the younger men in the profession in mind. The dues have been kept low, well within the financial range of the younger man who may not be able to afford the membership fee of the more expensive special medical societies. The association affords an opportunity not only to attend medical meetings but also to present the results of individual research. Certainly the younger men should have the opportunity of this form of stimulation and contact, and the holding of these meetings the day before the meeting of the Section on Ophthalmology of the American Medical Association stimulates interest in the section papers and exhibits. Derby[5] and Feingold[6] are former chairmen who in their presidential addresses stressed the value of attending medical meetings.

Every young ophthalmologist should join his county medical society and participate actively in the work, especially in these trying days for the world and medicine and the days to come, which can hardly be less difficult.

Every ophthalmologist should be interested in the prevention of blindness and should take an active part in the work of local societies as well as in the activities of the National Society for the Prevention of Blindness. They should interest themselves in the ophthalmologic public relations committees of the state and county medical societies, if they have been organized, or help to organize them, so that they can improve the standards of ophthalmology.

The mere existence of ethical standards cannot raise the standards of the practice of ophthalmology. The problem is more fundamental, and it is my belief that more attention should be given to selecting men for medical and ophthalmologic training because of their excellent character in addition to scientific or scholastic proficiency.

CONCLUSIONS

Because of changed conditions resulting from the war and awakened social consciousness, ophthalmologists have an important part to play in furnishing better medical service to low income groups. The needs and hopes of the free people in the world must and will be met. We may look to medicine to continue to provide unselfish leadership, scientific study and intelligent planning.

4. Berens, C.: Medical Research in Connection with Ophthalmologic Hospitals and Clinics, Am. J. Ophth. **7**: 55, 1924.

5. Derby, G. S.: Standards of Ophthalmology, Tr. Sect. Ophth., A. M. A., 1924, p. 17.

6. Feingold, M.: The Habit of Attending Medical Meetings, Tr. Sect. Ophth., A. M. A., 1925, p. 17.

The future of ophthalmology lies in the hands of the younger men. It is the privilege and great responsibility of the senior ophthalmologists to train and guide their younger confrères, who should be stimulated and encouraged to assume leadership in formulating plans for medical service, research and the teaching of ophthalmology in the future. I am confident that leaders will be developed who will carry the fine tradition of American medicine and ophthalmology to even greater heights.

35 East Seventieth Street, New York 21.

CLINICAL USE OF PRODUCTS OF HUMAN PLASMA FRACTIONATION

I. ALBUMIN IN SHOCK AND HYPOPROTEINEMIA II. γ-GLOBULIN IN MEASLES

CHARLES A. JANEWAY, M.D.
BOSTON

PART I. ALBUMIN IN SHOCK AND HYPOPROTEINEMIA [1]

A. PLASMA FRACTIONATION

As our understanding of the mechanisms of disease has advanced, the compound empirical remedies of an earlier era in medicine have been steadily replaced by specific drugs. Human blood is undergoing similar evolution as a therapeutic agent. Blood is a complex mixture of cellular elements and protein components in a menstruum which closely corresponds in composition to the interstitial fluid of the body. It is a specific remedy for one condition—hemorrhage—but has been used in the past as a "shotgun" remedy for general debility, anemia, hypoproteinemia, infection and hemorrhagic tendency. In many of these conditions only one particular component of blood is needed.

The aim of the program of plasma fractionation is to supply the various protein components of plasma in concentrated and safe form for clinical use. This program had its origins in the needs of the armed forces for a compact, stable blood substitute for emergency use in situations where the saving of space and time was of prime importance. This led to the development of concentrated human serum albumin by Cohn, Oncley, Strong, Hughes and Armstrong [2] from blood collected by the American Red Cross. In the preparation of human albumin, other protein fractions were obtained and studies have been directed constantly toward improvements in the products derived from them and to their wider clinical application.

Table 1 presents schematically the various derivatives of whole blood and their clinical indications. The use of resuspended red cells, which should be an integral part of any program for the efficient utilization of human blood, has been studied both here and abroad by a number of investigators.[3] It should be emphasized that the clinical uses for plasma fractionation products listed in table 1 are only those which have been proved. Much remains to be done, but it is clear that the process of separating human blood into its functional components has already provided the clinician with useful tools for the treatment and study of disease.

B. CONCENTRATED HUMAN SERUM ALBUMIN [4]

The albumin molecule differs from the molecules of the globulins in size, charge and shape. Its smaller size (molecular weight 70,000) and greater net charge account for its high colloid osmotic pressure, while its more symmetrical shape accounts for its relatively low viscosity in solution.[5] The stability of albumin, particularly under optimal conditions,[6] has been an important factor in its usefulness for military purposes, since it can be shipped and stored without refrigeration. Because of its high solubility, it is possible to prepare concentrated solutions in water, glucose, saline solution or any other desired aqueous medium.

Although the use of albumin dissolved in water, glucose or other diluents has many interesting possibilities, most of our knowledge has been gained with the albumin solution dispensed in the standard Army and Navy package—25 per cent solution (25 Gm. in 100 cc.) in 1.7 per cent sodium chloride with merthiolate 1 : 10,000 as preservative.[7]

The immediate effects of an injection of concentrated albumin are (1) increase in serum albumin concentration and consequent (2) increase in colloid osmotic pressure of the plasma. The latter leads to (3) rapid transfer of fluid from the extravascular to the vascular compartment with (4) increase in plasma volume, (5) fall in hemoglobin and hematocrit and subsequent return of (6) serum albumin concentration and (7) colloid osmotic pressure toward normal. If the blood volume is depleted before albumin injection, as in shock, the fall in hemoglobin and hematocrit and increase in plasma volume will be sustained. If the blood volume is normal before albumin, then the plasma volume increase will be in excess of normal and the hemodilution will

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Read before the Section on Pathology and Physiology at the Ninety-Fourth Annual Session of the American Medical Association, Chicago, June 14, 1944.

This work has been carried out under contract recommended by the Committee on Medical Research between the Office of Scientific Research and Development and Harvard University.

This paper is No. 30 in the series "Studies on the Plasma Proteins" from the Harvard Medical School, Boston, on products developed in the Department of Physical Chemistry from blood collected by the American Red Cross.

1. This paper is a condensed summary of work which has been done by a very large group of investigators, both in the laboratory and in the clinic. For detailed reports of the various studies on the products of plasma fractionation, the reader is referred to a series of papers on "Chemical, Clinical and Immunological Studies of the Products of Human Plasma Fractionation" (J. Clin. Investigation **23**, July 1944).

2. Cohn, E. J.; Oncley, J. L.; Strong, L. E.; Hughes, W. L., Jr., and Armstrong, S. H., Jr.: Chemical, Clinical and Immunological Studies on the Products of Human Plasma Fractionation: I. The Characterization of the Protein Fractions of Human Plasma, J. Clin. Investigation **23**: 417-433 (July) 1944.

3. Taylor, E. S.; Thalhimer, W., and Cooksey, W. B.: The Organization of a Red Blood Cell Transfusion Service, J. A. M. A. **124**: 958-960 (April 1) 1944. Cooksey, W. B., and Horwitz, W. H.: Use of Salvaged Red Cells, ibid. **124**: 961-964 (April 1) 1944.

4. In this section the author has attempted to summarize existing knowledge concerning the uses of concentrated human serum albumin. Most of this has been gained from work carried on by my colleagues Lieut. Comdrs. L. M. Woodruff and S. T. Gibson (MC), U.S.N.R., Capt. L. R. Newhouser (MC), U.S.N., Lieut. J. T. Heyl (MC), U.S.N.R., Dr. O. T. Bailey and Dr. J. G. Gibson 2d. An initial evaluation of albumin in the treatment of shock (reported by Woodruff and Gibson [12]) led to the production of albumin for the Army and Navy under Navy contract. Since then the observations on the use of albumin in hypoproteinemia have been a by-product of a program to test commercial lots of albumin for acceptance by the Navy. Consequently these studies have been somewhat fragmentary, since the pressing need of the armed forces for blood substitutes prevented the planning and execution of long range experiments. Detailed studies of the action of albumin in shock have been carried out under contracts with the Office of Scientific Research and Development by Cournand, Noble, Breed, Lauson, Baldwin, Pinchot and Richards [13] and by Warren, Stead, Merrill and Brannon,[13] whose work will be frequently referred to in the text.

5. Cohn, E. J.: The Plasma Proteins: Their Properties and Functions, Tr. & Stud., Coll. Physicians, Philadelphia **10**: 149-162 (Dec.) 1942.

6. Scatchard, G.; Gibson, S. T.; Woodruff, L. M.; Batchelder, A. C., and Brown, A.: Chemical, Clinical and Immunological Studies on the Products of Human Plasma Fractionation: IV. A Study of the Thermal Stability of Human Serum Albumin, J. Clin. Investigation **23**: 445-454 (July) 1944. Ballou, G. A.; Boyer, P. D.; Luck, J. M., and Lum, F. G.: Chemical, Clinical and Immunological Studies on the Products of Human Plasma Fractionation: V. The Influence of Nonpolar Anions on the Thermal Stability of Serum Albumin, ibid.

7. Newhouser, L. R., and Lozner, E. L.: The Use of Human Albumin in Military Medicine: III. The Standard Army-Navy Package of Serum Albumin Human (Concentrated), U. S. Nav. M. Bull. **40**: 796-799 (Oct.) 1942.

not be sustained but will diminish over a period of several hours as excess plasma protein leaves the blood stream. This is shown by changes in hemoglobin concentration in chart 1.

The advantages of albumin for use in shock and certain forms of hypoproteinemia are chiefly those of safety and convenience. Because of its stability, it can be transported and kept for long periods without refrigeration, while it occupies but little space. It is ready for instant injection without reconstitution, cross matching or other preliminary testing. Its safety has been borne out by experience—and with the type of control used in its production and testing, reactions are almost unknown in clinical use. Its compactness is of great assistance in administering protein to children or to patients with poor veins. Thus, when it becomes available, albumin should be a very valuable addition to the emergency kit carried by the practitioner or kept in the accident room of a busy hospital.

Albumin is indicated in the treatment of conditions in which its high colloid osmotic pressure will be advantageous. At present we have data on its usefulness in two such groups of conditions—shock and hypoproteinemia.[8]

TABLE 1.—*Blood and Blood Derivatives*

Derivative	Fraction	Protein	Clinical Use
Whole Blood..... ↓ (centrifuged)	.....	.....	Hemorrhage
1. Resuspended RBC..... + (pooled)	.....	.....	Anemia
2. Pooled Plasma..... ↓ (fractionated)	.....	.....	Burns, hemophilia, prothrombin deficiency
1. Fibrin Film.....	I	Fibrinogen	Dural substitute
2. Fibrin Foam and Thrombin.....	III-2	β-Globulin.....	Hemostasis
3. γ Globulin Antibodies..	II	γ Globulin.....	Measles prophylaxis
4. Isohemagglutinins.....	III-1	β + γ-Globulins	Blood grouping
5. Albumin.....	V	Albumins.....	Shock, hypoproteinemia, edema
6. Other Fractions.....	IV	α + β-Globulins	To be determined

In shock, whether due to hemorrhage, trauma or burns, it restores the diminished blood volume toward normal by drawing on the extravascular fluids, and this is accompanied by clinical improvement. This has been demonstrated in dogs,[10] in human volunteers who submitted to large venesections [11] and in clinical cases of shock.[12] The blood volume changes after treatment with concentrated human albumin in a group of 14 patients with shock due to trauma, hemorrhage and burns are shown in chart 2. Osmotic pressure measurements indicate that each gram of albumin should hold the equivalent of 18 cc. of fluid in the circulation and a 5.6 per cent albumin solution should be isotonic with a 7 per cent plasma.[13] Thus 25 Gm. of albumin is osmotically equivalent to 450 cc. of circulating plasma

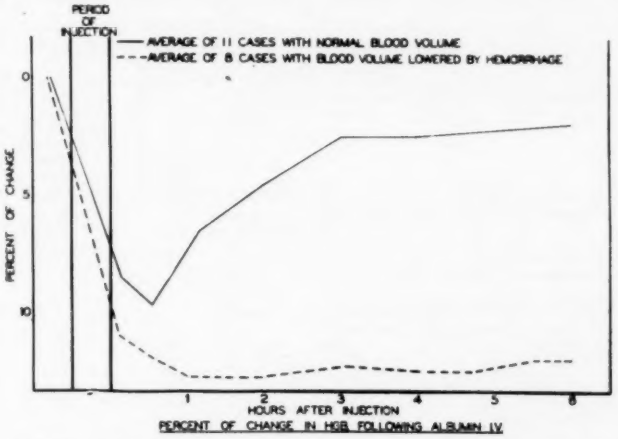
PERIOD OF INJECTION
AVERAGE OF 11 CASES WITH NORMAL BLOOD VOLUME
AVERAGE OF 8 CASES WITH BLOOD VOLUME LOWERED BY HEMORRHAGE
PERCENT OF CHANGE
HOURS AFTER INJECTION
PERCENT OF CHANGE IN HGB FOLLOWING ALBUMIN IV

Chart 1.—Contrast in the plasma volume change (as measured by the percentage change in hemoglobin concentration) after the injection of concentrated human serum albumin in a group of patients whose blood volumes had been depleted by acute hemorrhage and in a group with normal blood volumes. Note that immediate rapid hemodilution occurs in both groups (most normals received a smaller dose of albumin) but is sustained only in the group who had lost blood.

or 500 cc. of citrated plasma. That these theoretical considerations are well substantiated by actual clinical experience is shown in table 2. For this reason the standard Army and Navy package contains 25 Gm., which is equivalent to the standard Army and Navy package of dried human plasma (500 cc.) but is only about one sixth as heavy or as bulky. In treating cases of shock, 25 Gm. doses may be repeated at fifteen to

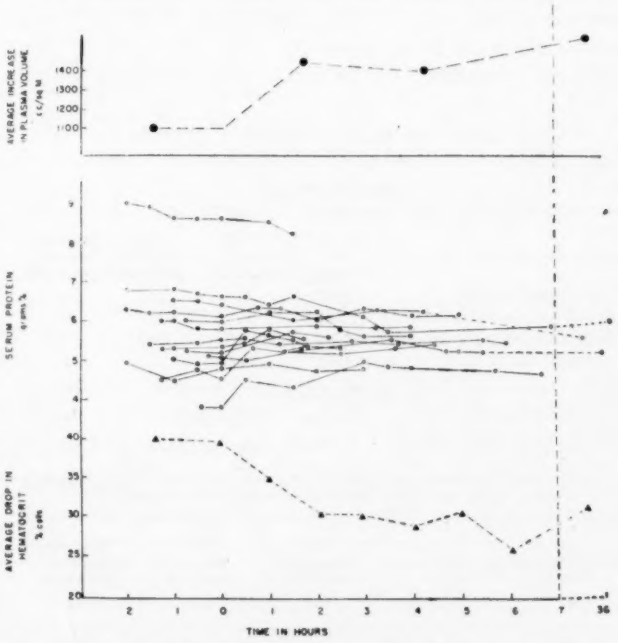

Chart 2.—Changes in plasma volume, serum protein concentration and hematocrit after injection of concentrated human serum albumin in 14 cases of shock due to hemorrhage, trauma and burns. (Reprinted from the Journal of Clinical Investigation, July 1944, p. 494, with permission of the authors [Cournand and others] and editors.)

8. Janeway, C. A.; Gibson, S. T.; Woodruff, L. M.; Heyl, J. T.; Bailey, O. T., and Newhouser, L. R.: Chemical, Clinical and Immunological Studies on the Products of Human Plasma Fractionation: VII. Concentrated Human Serum Albumin, J. Clin. Investigation **23**: 465-491 (July) 1944.

10. Dunphy, J. E., and Gibson, J. G., 2d: The Effect of Infusions of Bovine Serum Albumin in Experimental Shock, Surgery **14**: 509-518 (Oct.) 1943. Fine, Frank and Seligman.[14]

11. Stead, E. A., Jr., and Ebert, R. V.: Studies on Human Albumin, in Mudd, S., and Thalhimer, W.: Blood Substitutes and Blood Transfusion, Springfield, Ill., Charles C Thomas, Publisher, 1942, p. 185. Heyl, J. T.; Gibson, J. G., 2d, and Janeway, C. A.: Studies on the Plasma Proteins: V. The Effect of Concentrated Solutions of Human and Bovine Serum Albumin on Blood Volume After Acute Blood Loss in Man, J. Clin. Investigation **22**: 763-773 (Nov.) 1943.

12. Woodruff, L. M., and Gibson, S. T.: The Use of Human Albumin in Military Medicine: II. The Clinical Evaluation of Human Albumin, U. S. Nav. M. Bull. **40**: 791-796 (Oct.) 1942. Warren, J. V.; Stead, E. A., Jr.; Merrill, A. J., and Brannon, E. S.: Chemical, Clinical and Immunological Studies on the Products of Human Plasma Fractionation: IX. The Treatment of Shock with Concentrated Human Serum Albumin: A Preliminary Report, J. Clin. Investigation **23**: 506-510 (July) 1944. Cournand, A.; Noble, R. P.; Breed, E. S.; Lauson, H. D.; Baldwin, E. de F.; Pinchot, G. B., and Richards, D. W., Jr.: Chemical, Clinical and Immunological Studies on the Products of Human Plasma Fractionation: VIII. Clinical Use of Concentrated Human Serum Albumin in Shock, and Comparison with Whole Blood and with Rapid Saline Infusion, J. Clin. Investigation **23**: 491-506 (July) 1944.

13. Scatchard, G.; Batchelder, A. C., and Brown, A.: Chemical, Clinical and Immunological Studies on the Products of Human Plasma Fractionation: VI. The Osmotic Pressure of Plasma and of Serum Albumin, J. Clin. Investigation **23**: 458-465 (July) 1944.

thirty minute intervals, but, as with plasma, in traumatic cases whole blood or red cells must be given after large doses to correct the anemia which inevitably develops.

In patients in shock who are severely dehydrated, albumin will restore the amount of total circulating protein to normal without harm to the patient, but unless the salt and water necessary to make up the deficit of fluid in both plasma and extracellular fluid are administered, the therapeutic effect will obviously be inadequate. This has been our experience in only a few cases of shock in civilian hospitals, all of which were caused by serious intra-abdominal disease in which vomiting had depleted the body fluids. Work on dogs [14] has borne this out.[15] The additional fluid does not necessarily have to be given by vein but may be given orally, if tolerated, or by any other available route.

TABLE 2.—*Osmotic Effect of Concentrated Human Serum Albumin*

Authors	No. Cases	Hours After Albumin	Average Cc. Blood Volume Increase per Gm. of Albumin
Scatchard, Batchelder and Brown [13]	Calculated from Osmotic Pressure		18
Heyl, Gibson and Janeway [11]..... (Experimental hemorrhage)	11	1	17*
Cournand, Noble, Breed, Lauson, Baldwin, Pinchot and Richards: J. Clin. Investigation **23**: 491, [July] 1944	4†	1-2	19‡
(Clinical shock).....	12	1-36	23‡
Warren, Stead, Merrill and Brannon [12] ..... (Clinical shock)	3	½-1	16*

* Per gram of albumin injected (no bleeding after injection).
† These cases selected from group for comparison, since determinations were made within two hours of albumin injection.
‡ Per gram of albumin retained (11.2 cc. per gram of albumin injected).

TABLE 3.—*Effectiveness of γ-Globulin Compared to Other Preparations Used in the Prophylaxis of Measles*

(Unselected cases)

	No. Cases	No Measles, per Cent	Mild Measles, per Cent	Average Measles, per Cent
Convalescent serum.....	1,627	75	17	8
Normal adult serum.....	584	56	24	20
Placental extract.....	2,740	64.3	30.4	5.3
γ-Globulin	2,521	71.5	25.1	3.4

TABLE 4.—*Effectiveness of γ-Globulin in Measles Tests*

(Selected cases: Intimate exposure, 12 years of age and under, injection before tenth day after initial exposure, satisfactory data)

No. Preparations Tested	No. Cases	No Measles, per Cent	Mild Measles, per Cent	Average Measles, per Cent
40	1,168	65.8	31.3	2.9

The absence of the globulin components of plasma has not affected the usefulness of albumin in our experience with 100 shock cases, with 1 exception, a patient with a 50 per cent burn, in whom continued replacement with 300 Gm. of albumin in eighteen hours led to hypoglobulinemia, which was readily corrected with plasma.[8] The place of albumin in the treatment of shock is particularly in its early phases, when the emergency demands prompt restoration of blood volume, and in those cases in which peripheral circulatory failure is related to hypoproteinemia with edema. In the treatment of burns, plasma should be used to replace the losses of whole plasma, although albumin will carry patients through the first twelve hours if necessary.

The usefulness of albumin in the treatment of hypoproteinemia and edema remains to be explored to a large extent.[8] Although we have given albumin in 25 Gm. doses daily for long periods of time to a number of hypoproteinemic patients, we have had an opportunity in only a few patients to use large doses in a short time, which seem essential for most efficient correction of hypoalbuminemia. In a number of cases of burns which had developed a syndrome of hypoproteinemia, edema and failure of the peripheral circulation as a result of treatment with large amounts of saline solution the infusion of 50 Gm. of albumin led to dramatic improvement. Chart 3 shows the results of administration of 25 Gm. of albumin in four days to a baby with hypoproteinemia associated with weeping eczema of two weeks' duration. The rapid decline in weight was accompanied by diuresis and disappearance of the edema and ascites, which were presumably due to hypoalbuminemia and aggravated by the administration of sodium bicarbonate. Thorn [16] has emphasized the possible usefulness of albumin in cases of renal insufficiency with hypoproteinemia to raise the colloid osmotic pressure, thus increasing blood volume and glomerular filtration, and to supply protein without increasing the load of nonprotein nitrogen for the kidney to clear.

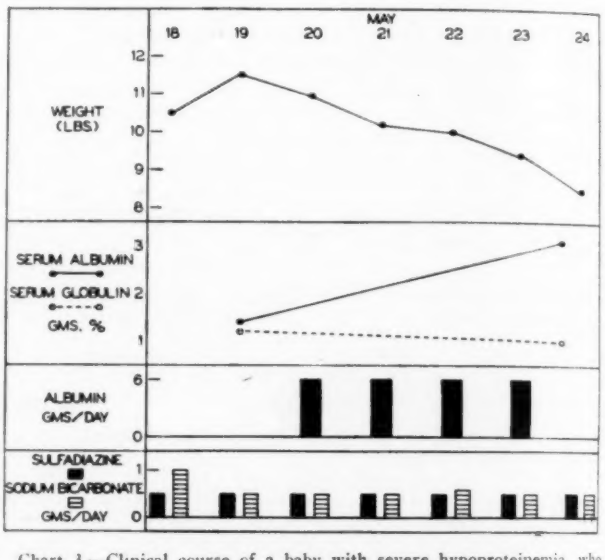

Chart 3.—Clinical course of a baby with severe hypoproteinemia, who was given concentrated human serum albumin 6.25 Gm. (25 cc.) per day for four days. On May 19 the baby had severe anasarca and ascites, while on May 24 only slight edema remained about the area of infection on the forehead and scalp.

In certain chronic types of hypoproteinemia, albumin administration will increase the concentration of serum albumin if sufficiently large amounts are given. When doses of only 25 Gm. daily are used, a great deal must be given and only a small portion can be accounted

14. Fine, J.; Frank, H. A., and Seligman, A. M.: Traumatic Shock: VIII. Studies in the Therapy and Hemodynamics of Shock, J. Clin. Investigation **23**: 731-741 (Sept.) 1944.
15. Mahoney, E. B., and Howland, J. W.: Personal communication to the author.
16. Thorn, G. W.: Physiologic Considerations in the Treatment of Nephritis, New England J. Med. **229**: 33-48 (July 8) 1943.

for in the peripheral circulation. The remainder is presumably stored or utilized while sparing other proteins, since no increase in nonprotein nitrogen excretion was observed in 3 hypoproteinemic patients whose nitrogen balance was studied during albumin therapy. In several cases of cirrhosis of the liver it has been possible to raise the level of serum albumin and to reduce the serum globulin by doses of 25 Gm. daily. In these patients some general improvement was noted, but no conclusions could be drawn concerning the control of ascites. When albumin injections were discontinued, the serum albumin level fell again within a month or two.

In patients with the nephrotic syndrome the administration of albumin was promptly followed by an increased excretion of protein in the urine.[17] In certain patients no improvement was noted; in 2 children, however, the administration of very large amounts (500 Gm. to a 16 month old child in twenty days; 560 Gm. to a boy of 8 in a month) coincided with diuresis and decided clinical improvement, although in other patients this did not occur. Since the results have been irregular, this problem requires much more careful study.

TABLE 5.—*Use of γ-Globulin in Measles Prophylaxis in Adolescents and Adults (Over 12)*

(Combined figures for 1942-43, 1943-44 seasons)

	Total	No Measles	Mild Measles	Average Measles
Intimate exposure	106	71 (67%)	30 (28%)	5 (5%)
Moderate or casual exposure	106	97 (92%)	8 (7%)	1 (1%)

Comment

1. Dose 5 cc. in most cases.
2. Day of injection varied from 1 to 9 days after exposure, chiefly 4 to 6 days.
3. Attack rate in age group 10 to 14 as reported by previous workers varies from 50 per cent to 15.4 per cent. Most of our patients were over 16.
4. The low attack rate makes evaluation difficult, but the fact that mild measles was more common than average measles in each group, whereas measles is usually severe in adolescents and adults, indicates that the globulin has had an effect.

In the treatment of hypoproteinemia with large doses of albumin, the powerful osmotic effect of albumin must be borne in mind. The patient should be watched for signs of venous and pulmonary congestion, and observation of the hemoglobin or hematocrit should enable the physician to follow the trend of the plasma volume over short periods. We have been impressed with how well large doses of albumin are tolerated, perhaps because of the low viscosity, but we observed 1 seriously ill elderly patient in whom doses of from 75 to 125 Gm. per day (650 Gm. in six days) appeared to exceed the limits of compensation.

SUMMARY TO PART I

1. By the application of large scale methods of fractionation developed in the Department of Physical Chemistry of the Harvard Medical School to pooled human plasma from blood collected by the American Red Cross, concentrated human serum albumin, γ-globulin antibodies, isohemagglutinins, fibrin films and fibrin foam with thrombin have been made available for clinical use.

2. Concentrated human serum albumin, as dispensed in the standard Army and Navy package, provides a compact, stable solution ready for immediate use in the emergency treatment of shock.

3. The use of albumin in cases of shock due to hemorrhage, trauma and burns results in an increase in blood volume, hemodilution and clinical improvement. The blood volume is increased in these conditions by approximately the amount to be expected from measurements of its osmotic pressure (18 cc. per gram of albumin).

TABLE 6.—*Complications of Measles in Children Under 12 Receiving γ-Globulin*

(1,168 injections: 366 cases of mild measles, 34 cases of average measles)

Age	Dose Cc./Lb.	Days from Exposure to Injection	Result	Complications
2 yrs.	.02	9	Severe measles	Staphylococcus aureus pneumonia and empyema with recovery
11 mos.	.025	6	Average measles	Mild encephalitis with recovery
2 yrs.*	.025	..	Average measles	Otitis media (simple)

* Child had reaction with chills, fever and edema of eyelids day after injection of globulin.

TABLE 7.—*Reactions from Injection of γ-Globulin in Measles Prophylaxis*

Type of Reaction	No. Cases	No. Reactions	Per Cent of Total Reactions
Local soreness or swelling	16	16	50
Fever	11	12	38
Headache	1	1	3
Dizziness	1	1	3
Hyperactivity	1	1	3
Chills, fever, orbital edema *	1	1	3
Totals	31	32	100

Summary

1,843 injections; 32 reactions in 31 patients.
1.7 per cent reactions; one half local and one half general, chiefly fever, with one anaphylactoid type of reaction.*

TABLE 8.—*Results in Young Adults with 5 Cc. Dose of γ-Globulin*

(Stokes and Maris)

Group	No. Cases	No Measles	Mild Measles	Average Measles
Immunized	65	54 (83%)	10*	1 (1.5%)
Controls	42	20 (48%)	4†	18 (42%)

* Very mild measles in 8, questionable measles in 2 (catarrhal symptoms and fever, but no rash).
† These cases more severe than in immunized group.

4. In the presence of severe dehydration, albumin must be supplemented with fluids in order to obtain the maximum therapeutic effect.

5. Albumin is an extremely safe blood derivative and can be administered very rapidly without reaction even after periods of heating at temperatures of 50 C. for as long as one hundred days.

6. Albumin can be used to correct hypoproteinemia if sufficiently large amounts are used.

17. Luetscher, J. A., Jr.: The Effect of a Single Injection of Concentrated Human Serum Albumin on Circulating Proteins and Proteinuria in Nephrosis, J. Clin. Investigation **23**: 365-371 (May) 1944. Janeway, Gibson, Woodruff, Heyl, Bailey and Newhouser.[8]

7. In the nephrotic syndrome the injection of albumin is followed by a definite increase in proteinuria but does not regularly result in a diuresis.

PART II. γ-GLOBULIN IN MEASLES[18]

Normal serum γ-globulin antibodies (human) concentrated (immune serum globulin) have been prepared as a plasma fractionation product from blood collected by the American Red Cross by the methods of Cohn, Oncley, Strong, Hughes and Armstrong.[2] About 60 per cent of the antibodies are recovered in fraction II and appear to be γ-globulins, which comprise 96 per cent or more of the protein of recent preparations. Robinson[19] early suggested that this globulin fraction from pooled normal plasma might be effective in the prevention and modification of measles.

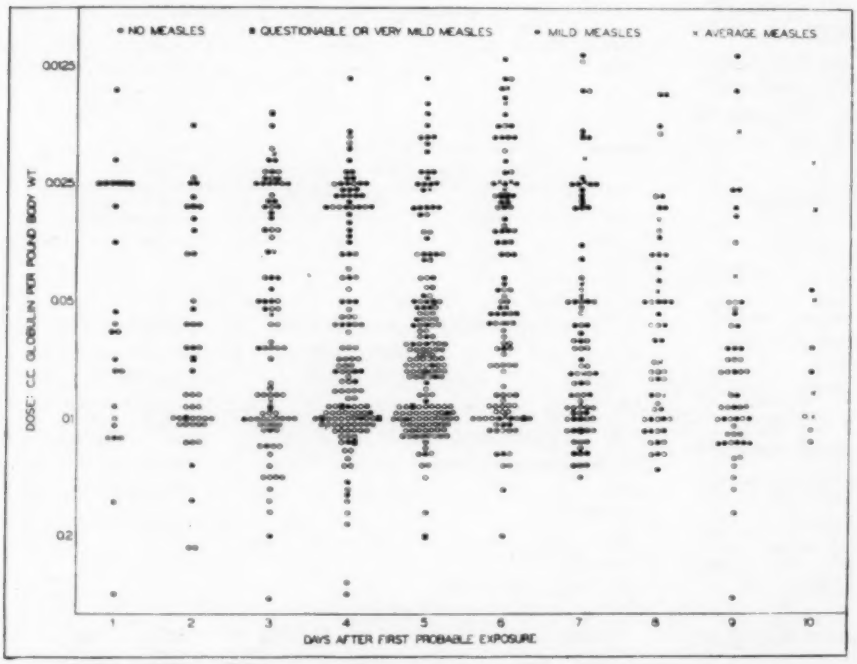

Chart 4.—Results in 837 satisfactory prophylactic injections of γ-globulin, as influenced by the size of the dose in terms of body weight and by the interval between injection and first probable exposure.

Enders[20] has reported on the concentrations of the great variety of antibodies which have been detected in γ-globulin preparations (fraction II). In these preparations most antibodies are concentrated approximately 25-fold over the pooled plasma from which they are derived. Variations in antibody titers from one preparation to another are slight, since the initial pool consists of the plasma from 2,000 to 4,000 donors, and the variations which do occur presumably reflect variations in the antibody levels of the population from whom the blood was drawn.

Proof that fraction II is a safe and effective agent for the prevention and modification of measles was obtained in 1943 by Stokes, Maris and Gellis[21] and confirmed by Ordman, Jennings and Janeway.[22] It is now being produced under Navy contract for the Army and Navy, and it has been our concern this year to test each preparation produced for its effectiveness against measles. Final tests of the material as a prophylactic agent against measles were carried out in children under 12 who were intimately exposed to the disease in the home, since it is known that the attack rate under such conditions is very high.[23] All injections were given intramuscularly. Reports were sent to a central office at least three weeks after injection, where the results were tabulated and analyzed.

RESULTS

1. *Effectiveness of γ-Globulin.*—Table 3 presents the comparison of γ-globulin with other agents used in measles prophylaxis in unselected cases.[23a] Table 4 gives the results of the measles testing program for the satisfactory cases (children under 12, intimate home exposure, adequate follow-up data, injection before the tenth day after exposure).

We have been particularly anxious to ascertain the effectiveness of globulin in adults, a difficult problem, since the attack rate is low in this age group. Table 5 gives the results in 212 exposed and supposedly susceptible adolescents and adults.

2. *Complications.*—The rationale for attempting to modify measles is based on two premises: first, that modified measles confers a lasting immunity and, second, that the modified disease is much less serious. Proof of the first premise cannot be obtained as yet, but evidence for the second is available. Since the fatalities and serious sequelae from measles are usually associated with the development of complications, it is important to learn whether complications are less frequent in modified measles. In table 6 are listed the complications observed in a group of 1,168 children fulfilling our criteria for a satisfactory test of the globulin. The outstanding finding is that the only 3 complica-

18. The studies reported in this section would not have been possible without the cooperation of a number of agencies and individuals. Much of the work in Boston in 1943 was carried on by Dr. Charles W. Ordman. Field tests of globulin preparations against measles in 1944 have been carried out with the assistance of the Commission on Measles and Mumps, Board for the Investigation and Control of Influenza and Other Epidemic Diseases in the Army, in Philadelphia and Baltimore under the direction of Dr. Joseph Stokes Jr., Dr. Elizabeth P. Maris and Lieut. S. S. Gellis, M. C., A. U. S.; in New York City, through the Department of Health, by Dr. Maurice Greenberg, Dr. Samuel Frant and Dr. David D. Rutstein; in Washington, D. C., under Capt. L. R. Newhouser (MC), U.S.N., and Dr. Lewis K. Sweet; in Durham, N. C., under Dr. W. C. Davison, and in Boston and vicinity with the cooperation of the Massachusetts Department of Health, the Massachusetts Antitoxin and Vaccine Laboratory and the Health Officers of Arlington, Medford, Malden and Chelsea. We are indebted to the large number of physicians in Boston, New York, Philadelphia, Baltimore, Washington and Durham who have provided most of the reports on which this study is based; to Dr. William B. Berenberg and the house and resident staff of the Children's Hospital for their assistance in the control and distribution of globulin, and to Miss Virginia S. Poole, B.S., who has kept the records, tabulated the data and prepared the charts for this report.

19. Cohn, E. J.; Luetscher, J. A., Jr.; Oncley, J. L.; Armstrong, S. H., Jr., and Davis, B. D.: Preparation and Properties of Serum and Plasma Proteins: III. Size and Charge of Proteins Separating on Equilibration Across Membranes with Ethanol-Water Mixtures of Controlled *pH*, Ionic Strength and Temperature, J. Am. Chem. Soc. **62**: 3396-3400, 1940; see footnote, p. 3398.

20. Enders, J. F.: Chemical, Clinical and Immunological Studies on the Products of Human Plasma Fractionation: X. The Concentrations of Certain Antibodies in Globulin Fractions Derived from Human Blood Plasma, J. Clin. Investigation **23**: 510-531 (July) 1944.

21. Stokes, J., Jr.; Maris, E. P., and Gellis, S. S.: Id. XI. The Use of Concentrated Normal Human Serum γ-Globulin in the Prophylaxis and Treatment of Measles, J. Clin. Investigation **23**: 531-541 (July) 1944.

22. Ordman, C. W.; Jennings, C. G., Jr., and Janeway, C. A.: Id. XII. The Use of Concentrated Normal Human Serum γ-Globulin for the Prevention and Attenuation of Measles, J. Clin. Investigation **23**: 541-550 (July) 1944.

23. Stillerman, M., and Thalhimer, W.: Attack Rate and Incubation Period of Measles, Am. J. Dis. Child. **67**: 15-21 (Jan.) 1944.

23a. The figures for convalescent serum, normal adult serum and placental extract in table 3 are from McKahn, C. F.: The Prevention and Modification of Measles, J. A. M. A. **109**: 2034 (Dec. 18) 1937.

tions observed were in cases in which the attempt to modify the disease apparently failed, as typical measles developed.

3. *Reactions.*—Most physicians who have previously used placental extract for measles prophylaxis have remarked on the low incidence of reactions following

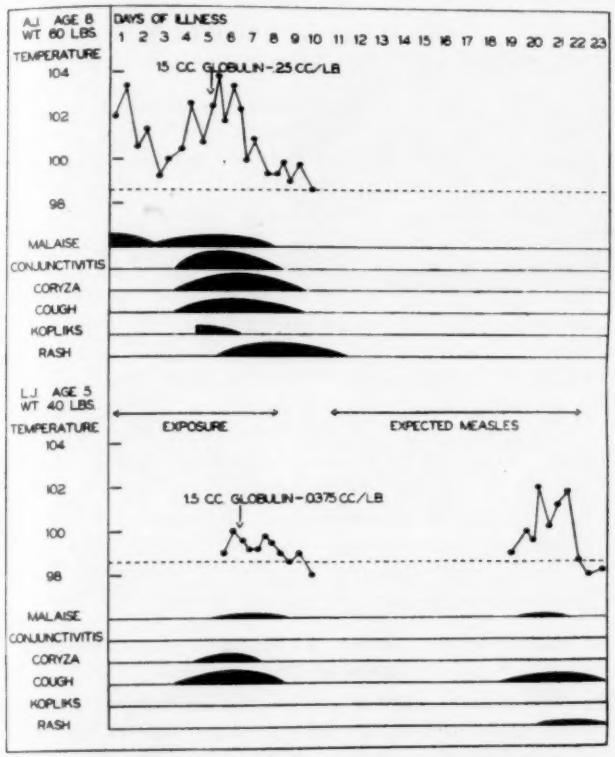

Chart 5.—Satisfactory modification of measles in a sibling intimately exposed to an older sister. The initial bout of fever in each patient may have been due to an intercurrent infection with short incubation period. The large dose of globulin given just before appearance of the rash in the older child appears to have had no effect. This has been our general experience, but Stokes, Maris and Gellis [21] feel that γ-globulin may be useful in the early treatment of measles. The rash in the modified case consisted of about 50 minute pink, maculopapular lesions and might have been readily overlooked.

the use of γ-globulin. The reactions reported in 1,843 intramuscular injections are presented in table 7.

4. *Dosage and Time of Injection.*—In the reports based on clinical trials in 1943, both groups of authors [24] came to essentially similar conclusions concerning dosage. With the large number of satisfactory reports accumulated in two seasons, it has been possible to confirm the validity of these recommendations concerning the proper dosage of γ-globulin. Study of charts 4 and 6 will show very clearly that, whereas the results in the first eight days after exposure are directly dependent on the dose of globulin (calculated on a weight basis), the interval between exposure and injection makes much less difference, although the number of cases of mild and average measles increases after the fifth day. In other words, if complete protection is desired, give 0.1 to 0.075 cc. per pound as early as possible; if modification is desired, use one fourth of this dose (0.025 to 0.02 cc. per pound) on the fourth or fifth day. The fifth day after exposure is the usual time of administration in the home, since it is the day on which the rash usually appears in the source case. These dosage recommendations will give at best only about 80 per cent satisfactory results, since the susceptibility of the individual, as emphasized by Stokes, Maris and Gellis,[21] is an important variable. This is brought out by the exceptional cases in chart 4.

The proper dosage for adults is difficult to determine. Stokes and Maris [25] have had the opportunity to make a controlled study in a group of 107 presumably susceptible college students who were exposed to active cases of measles in several meetings. A dose of 5 cc. was given to 65 of the group and 42 were not immunized. The results are shown in table 8. This suggests that the dosage schedule worked out on a weight basis for children may be applicable to adults, since the average dose used in this group was 0.04 cc. per pound, one which would be expected to give results similar to those obtained.

5. *Mild Measles.*—The modified form of measles which results after a proper dose of γ-globulin does not differ from that previously described. Most cases are milder in all respects and briefer in duration than typical cases. Each of the cardinal symptoms—catarrh, fever, malaise and rash (including exanthem)—may occur alone or in conjunction with the others, and with varying degrees of severity. Since rash is usually accepted as an essential feature of the disease, it is hard to classify cases with fever, cough and coryza occurring twelve to fourteen days after exposure, but at least 14 such cases occurred in the group reported. Close observation of the patient is usually necessary between the ninth and twentieth days after exposure if mild measles is to be recognized, as the rash may be sparse and transitory, and the fever short lived and unaccompanied by prostration. Chart 5 illustrates satisfactory modification of measles after home exposure.

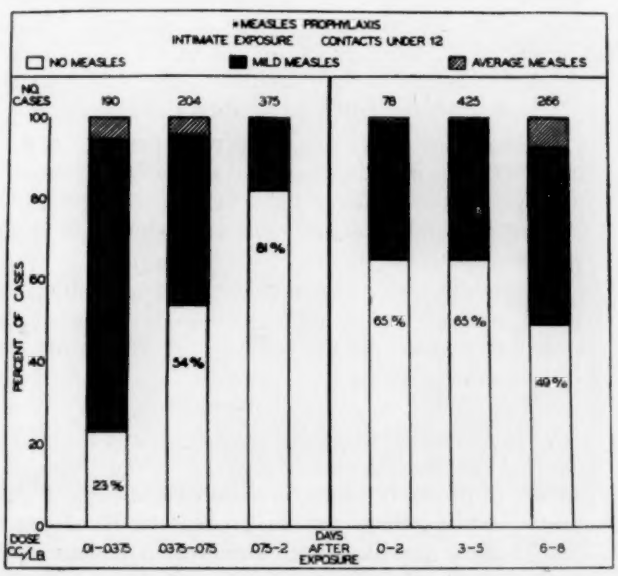

Chart 6.—Graphic summary of the data in chart 4. On the left is shown the relationship between the results and the size of the dose in patients injected within eight days of exposure. On the right is shown the relationship between the results and the time of injection regardless of the size of the dose.

6. *Duration of Immunity.*—It is probable that the duration of passive immunity depends to a considerable extent on the dose given. Evidence from last year's work indicates that a large dose (0.1 cc. per pound)

24. Stokes, Maris and Gellis.[21] Ordman, Jennings and Janeway.[22]

25. Stokes, J., Jr., and Maris, E. P.: Personal communication to the author.

confers immunity for at least three weeks [22] and that a 5 cc. dose in adolescents does not protect after six to eight weeks.

7. *Use of γ-Globulin in Institutions.*—Communicable diseases are a particular problem in institutions caring for children. The two diseases which cause the greatest difficulty in pediatric wards because of their contagiousness are measles and chickenpox. γ-globulin has proved extremely useful in controlling outbreaks of measles in pediatric wards. It has been given in thirty-five separate outbreaks to 350 susceptible children with the following results: not followed 95, no measles 241 (94.6 per cent), mild measles 13 (5 per cent), average measles 1 (0.4 per cent).

Unfortunately, a few limited trials in outbreaks of chickenpox suggest that it does not protect satisfactorily against this disease, at least in doses of 5 to 20 cc.

SUMMARY OF PART II

1. γ-globulin antibodies (fraction II of Cohn, Strong, Oncley, Hughes and Armstrong) contains most of the antibodies of pooled normal human plasma in 25-fold concentration over the original plasma.

2. γ-globulin antibodies is the safest and most effective agent available for the prevention and modification of measles by passive immunization.

3. For this purpose the injection should be given preferably on the fifth day after exposure. At this time a dose of 0.1 to 0.075 cc. per pound will completely protect most susceptible individuals, while one of 0.025 to 0.02 cc. per pound will result in mild measles in most cases.

4. The mild measles in patients receiving globulin is similar to that previously observed in patients immunized with convalescent serum or placental extract. Complications were noted in 3 out of 400 cases of measles in immunized children but occurred in patients in whom globulin failed to modify the disease.

5. Reactions were noted in only 1.7 per cent of 1,843 intramuscular injections. Half of these consisted of local soreness and most of the remainder of fever. Only one anaphylactoid reaction occurred, which was probably due to an idiosyncrasy.

6. γ-globulin is very effective in controlling the spread and severity of measles in pediatric wards but does not appear to be effective in the control of chickenpox.

CONCLUSIONS

1. Fractionation of pooled human plasma from blood collected by the American Red Cross has yielded a number of products which have important clinical applications, while others are in process of development. Two of these products are concentrated human serum albumin and γ-globulin antibodies, which are discussed in this paper.

2. Concentrated human serum albumin exerts its expected osmotic effect when injected into the blood stream and this may be utilized in the treatment of shock and hypoproteinemic edema. It is an extremely safe, convenient and effective blood derivative.

3. γ-globulin antibodies constitutes the safest and most effective agent available for the prophylaxis of measles.

CLINICAL USE OF PRODUCTS OF HUMAN PLASMA FRACTIONATION

III. THE USE OF PRODUCTS OF FIBRINOGEN AND THROMBIN IN SURGERY

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AND
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BOSTON

In the course of large scale fractionation of human blood plasma in the Department of Physical Chemistry at the Harvard Medical School [1] purified fractions of human fibrinogen and thrombin have become available in large amounts. From these proteins, several materials have been prepared for use in surgery; these materials have a wide variety of physical properties and differ greatly in the surgical uses for which they are adapted. Two products have thus far proved satisfactory in clinical and experimental trials and are now ready for distribution. One is fibrin foam, which is used with a solution of thrombin as an absorbable hemostatic agent. Another is fibrin film, which has been employed as a dural substitute and in the prevention of meningocerebral adhesions. To a less extent the solutions of fibrinogen and thrombin have been used directly in certain special locations, where they provide a physiologic adhesive material by virtue of the clot produced when they are mixed in situ.

FIBRIN FOAM WITH THROMBIN, AN ABSORBABLE HEMOSTATIC AGENT

The importance of hemostasis in surgery has been recognized as long as surgery itself has existed. Use of the ligature was known to Celsus, and his description of it was doubtless copied from still earlier sources. New technics for hemostasis in recent times, such as the silver clip and electrocoagulation, have come chiefly from neurosurgical investigators and have gradually found their way into those operations of the general surgeon, where they save time or secure more accurate control of bleeding than do traditional methods. This course has again been followed in the studies of human fibrin foam with thrombin, which was first used to control bleeding in neurosurgical operations and now promises to have use in certain general surgical procedures.

The characteristics of fibrin foam and the range of properties which may be secured by changes in the conditions of manufacture have been described elsewhere.[2] The fibrin foam is prepared from human

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From the Surgical Services of the Children's and the Peter Bent Brigham hospitals and from the Departments of Surgery and Pathology, Harvard Medical School.

This work has been carried out under contract recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Harvard University.

This paper is number 31 in the series "Studies on Plasma Proteins" from the Harvard Medical School, Boston, on products developed by the Department of Physical Chemistry from blood collected by the American Red Cross.

1. Cohn, E. J.; Oncley, J. L.; Strong, L. E.; Hughes, W. L., and Armstrong, S. H., Jr.: Chemical, Clinical and Immunological Studies on the Products of Human Plasma Fractionation: I. The Characterization of the Protein Fractions of Human Plasma, J. Clin. Investigation **23**: 417-432, 1944. Edsall, J. T.; Ferry, R. M., and Armstrong, S. H., Jr.: Chemical, Clinical and Immunological Studies on the Products of Human Plasma Fractionation: XV. The Proteins Concerned in the Blood Coagulation Mechanism, ibid. **23**: 557-565, 1944.

2. Bering, E. A., Jr.: Chemical, Clinical and Immunological Studies on the Products of Human Plasma Fractionation: XXII. The Development of Fibrin Foam as a Hemostatic Agent for Use in Conjunction with Human Thrombin, J. Clin. Investigation **23**: 586-590, 1944.

fibrinogen and thrombin and therefore is wholly composed of proteins native to human blood plasma. Its outstanding characteristics are that it rapidly controls bleeding from oozing surfaces and large veins and that it is absorbed with minimal tissue reaction when left in place at the end of an operation.

The fibrin foam has a honeycomb structure composed of fibrin with air spaces of various sizes (fig. 1). When it is to be used as a hemostatic agent, three bottles are supplied (fig. 2). One of these contains sterile fibrin foam, another dried human thrombin and the third 30 cc. of sterile isotonic solution of sodium chloride. At the time of use the saline solution is added to the dry thrombin; solution takes place rapidly. Pieces of fibrin foam are soaked in the thrombin solution and are then ready for use in hemostasis. The fibrin foam, which is firm and somewhat brittle in the dry state, becomes rubbery and shrinks as fluid enters the air spaces.

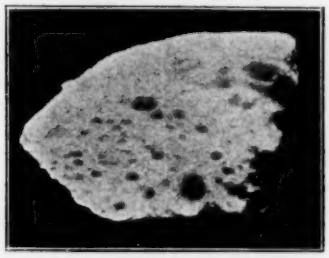

Fig. 1.—The appearance of fibrin foam before it has been soaked in thrombin solution. Note the porous structure.

The value of fibrin foam with thrombin as a hemostatic agent is greatly enhanced by the fact that it can be left in place. Absorption is rapid and the tissue reaction excited by the presence of the material is minimal from the point of view of the histologist and negligible from the point of view of the clinician. Since the fibrin foam remains on the bleeding surface after hemostasis is complete, it entirely obviates the recurrence of hemorrhage, so troublesome when cotton materials are removed from bleeding points.

FIBRIN FOAM WITH THROMBIN IN NEUROSURGERY

The use of fibrin foam with thrombin has greatly facilitated a variety of neurosurgical procedures. The bleeding from oozing surfaces may be controlled in other ways, but the rapidity and completeness of hemostasis secured with fibrin foam materially shortens the duration of operations in which this agent is used. Moreover, fibrin foam with thrombin stops bleeding under certain circumstances in which other methods have been unsatisfactory.

For use in any neurosurgical operation the dry fibrin foam is cut up into pieces of various sizes for use in the different types of bleeding which may be expected in that particular procedure. As the operation gets under way, these are placed in the thrombin solution so as to be ready for instant use. If minute fragments are wanted for control of small bleeding points, the moist fibrin foam can be picked up with forceps and cut or pulled apart. At the time when bleeding is encountered, a piece of the fibrin foam is selected and held firmly in place with a cotton pledget, which takes up excess moisture. Suction is often useful when applied over the pledget. It will then be possible to remove the pledget without dislodging the fibrin foam. The fragment can be molded somewhat to conform to the shape of the surface and will retain the configuration after excess moisture has been removed. Should additional hemostatic material be required because of unforeseen circumstances in the course of the operation, dry fibrin foam will be suitable for use after soaking in the thrombin solution for one minute.[3]

When dealing with blood vessel malformations or surfaces with bleeding from numerous small vessels, it is of advantage to slice the fibrin foam so that it forms a wafer thin plaque. The fibrin foam will not smear but retains the form into which it is pressed. Bleeding from spurting arteries is controlled with silver clips or ligatures. While fibrin foam is not recommended for brisk arterial bleeding, it will occasionally be satisfactory if applied with sufficient pressure. Fibrin foam with thrombin is also not recommended for the scalp, the cut edge of the dura or the cut edge of the bone. It is, however, of great value in dealing with bleeding from the dural sinuses and the large veins entering them. When pieces of fibrin foam are placed against torn dural sinuses or large tributary veins, control of bleeding is more effective than that secured by the use of muscle.

One of the situations in which fibrin foam has been found most useful is the outer surface of the dura beneath the margins of the bone flap. Here bleeding is often troublesome and its control may occupy considerable time. The fibrin foam can be tucked beyond the limits of the wound with safety and left in place.

Again, fibrin foam is extremely valuable in dealing with bleeding from the beds of cerebral neoplasms. By its use, certain large tumors can be removed when otherwise it might not be safe to resect them completely or to take them out en bloc when they would have to be dealt with piecemeal without this hemostatic agent. When a tumor of this sort is to be excavated or removed in toto, preparation is made by securing a large mass of fibrin foam, usually large enough to fill the entire cavity. If the cavity is larger than the largest piece of fibrin foam available, several smaller

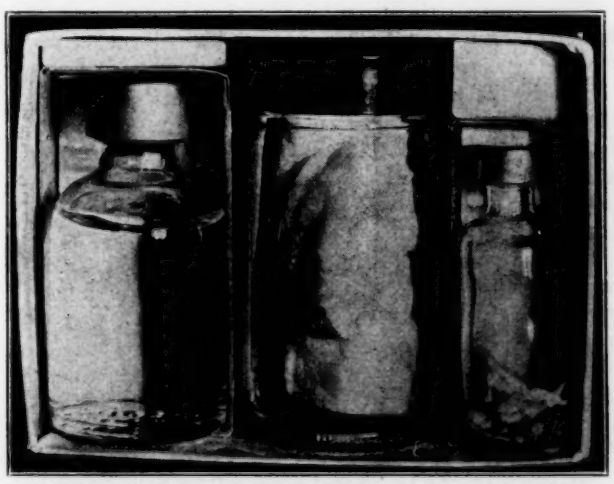

Fig. 2.—The package now in use for distribution of fibrin foam and thrombin. The center bottle contains dry fibrin foam. The right bottle contains dry thrombin and the left bottle isotonic solution of sodium chloride.

fragments may be pressed together. While the pieces of fibrin foam do not fuse, they adhere to one another well enough to make a compact ball. The application

3. Bailey, O. T., and Ingraham, F. D.: Chemical, Clinical and Immunological Studies on the Products of Human Plasma Fractionation: XXI. The Use of Fibrin Foam as a Hemostatic Agent in Neurosurgery; Clinical and Pathological Studies, J. Clin. Investigation **23**: 591-596, 1944. Ingraham, F. D., and Bailey, O. T.: The Use of Products Prepared from Human Fibrinogen and Human Thrombin in Neurosurgery: Fibrin Foams as Hemostatic Agents; Fibrin Films in Repair of Dural Defects and in Prevention of Meningocerebral Adhesions, J. Neurosurg. **1**: 23-39, 1944.

of several small bits of fibrin foam to a bleeding tumor bed would allow too much blood to accumulate among them. When the mass of fibrin-foam has been pressed against the tumor bed, its volume is reduced by excavating the center. A relatively thin but continuous coating of fibrin foam is thus left along the tumor bed.

We have now used fibrin foam with thrombin as a hemostatic agent in 169 neurosurgical operations. From this experience it appears to be a most valuable hemostatic agent. Use of human fibrin foam with thrombin at successive operations on one patient is not attended by any untoward results. The fibrin foam does not replace the cotton pattie as sponging material but finds its use in the control of bleeding. A new absorbable hemostatic agent has thus been added to a very restricted group of these materials now in common use.

By far the most widely used of the absorbable hemostatic materials is muscle, introduced by Cushing in 1911.[4] Fibrin foam with thrombin is superior in several important respects to muscle for this purpose.[5] The tissue reaction to fibrin foam with thrombin is much less than that elicited by muscle, as discussed in another part of this paper. Furthermore, the surgeon who uses muscle must content himself with the limited supply which he may obtain from the temporal muscle or perform another procedure to obtain additional material from the gastrocnemius or other muscle or depend on the chance that muscle may be secured from a concomitant operation, which is not always possible. On the other hand, fibrin foam with thrombin is ready in any amount and can be placed on the instrument table with as little concern as is given to the provision of an adequate supply of instruments. Should an emergency arise as the operation progresses, an additional supply is available in a few moments.

Fibrin foam with thrombin can also be more readily adapted to the particular bleeding area than can muscle. The foam is broken or cut to size with ease and may be molded further to fit contours once it has been placed. The structure of muscle prevents this degree of adaptability. Both muscle and fibrin foam are entirely of human origin and share the advantages of homologous materials when used for human patients.

In general, muscle has been reserved for emergencies by neurosurgeons. When serious hemorrhage occurs, such as that from a dural sinus or blood vessel malformation, hemostasis is better controlled by means of fibrin foam with thrombin than with muscle, and the large amount which must be used makes the minimal tissue reaction to fibrin foam an important consideration. Fibrin foam with thrombin finds perhaps its largest field of use in situations where muscle would seldom be employed. A great deal of time may be saved by the use of fibrin foam with thrombin to control oozing on the dura, beneath the edge of the bone flap and elsewhere. This saving of time amounts to at least half an hour and often to an hour or more in a single operation. Fibrin foam with thrombin has saved the life of some patients in whom large tumors had been removed when muscle would have been unsatisfactory as a hemostatic agent.

4. Cushing, H.: The Control of Bleeding in Operations for Brain Tumors, with a Description of Silver "Clips" for the Occlusion of Vessels Inaccessible to the Ligature, Ann. Surg. **54**: 1-19, 1911.

5. Ingraham, F. D.; Bailey, O. T., and Nulsen, F. E.: Studies on Fibrin Foam as a Hemostatic Agent in Neurosurgery, with Special Reference to Its Comparison with Muscle, J. Neurosurg. **1**: 171-181, 1944.

Soluble cellulose has been prepared for use as a hemostatic agent when soaked in thrombin solution.[6] After the demonstration by Frantz[7] that soluble cellulose is rapidly absorbed with minimal tissue reaction, it was used with thrombin for hemostasis in neurosurgery by Putnam.[8] Soluble cellulose and fibrin foam are both satisfactory from the standpoint of tissue reactions. While fibrin foam is made wholly from proteins of human origin, soluble cellulose is oxidized cotton. Our clinical experience with the two materials suggests that fibrin foam is superior to soluble cellulose as a hemostatic agent in neurosurgery. The control of bleeding by means of fibrin foam depends not only on the presence of thrombin but also on the way in which the thrombin is held in the honeycomb structure of the fibrin foam. Confirmation of this is seen in the fact that hemostasis is effected even when weak solutions of thrombin are used.[2] The loose structure of the soluble cellulose is less well adapted for the purpose and is not effective unless a considerably greater concentration of thrombin is available. Fibrin foam also has the advantage of being more easily cut and shaped to fit the individual characteristics of the bleeding point and especially of retaining the contours of the surface to which it is molded. From the standpoint of neurosurgery, the speed and tenacity with which fibrin foam adheres to tissues is very valuable. In our experience soluble cellulose has seemed less firmly adherent and the edges of the pledget have tended to curl away from the surface to which it has been applied.

Fibrin foam with thrombin has thus proved to be an effective absorbable hemostatic agent in many different types of neurosurgical operations.

TISSUE REACTION TO FIBRIN FOAM

It is of crucial importance that the tissue reactions caused by any absorbable material be minimal if its use is to be without danger in surgical procedures. Investigations of the tissue reactions to fibrin foam have been of two types—experimental studies, chiefly in monkeys, and studies of specimens removed at second operations or necropsies.[3]

Fibrin foam, as it comes in the bottle, appears microscopically to be composed of loose meshed fibers; these are actually cross sections of the honeycomb structure (fig. 3). When used as a hemostatic agent in conjunction with thrombin, the spaces fill with blood clot. This is followed by a shrinking and coalescence of the fibrin. The result is a minute mass of fibrin which persists for from one to four weeks (fig. 4). The absorption of the fibrin is accomplished by the intermediation of small numbers of mononuclear phagocytes and a few polymorphonuclear leukocytes. Giant cells occasionally form about the bits of fibrin. Fibrous tissue reaction is so slight that the location of the foam could usually not be identified in specimens obtained as late as one month after operation and often could not be located at much shorter intervals. These results are in conformity with the clinical observation that no untoward sequelae have been observed following the use of fibrin foam with

6. Yackel, E. C., and Kenyon, W. O.: The Oxidation of Cellulose by Nitrogen Dioxide, J. Am. Chem. Soc. **64**: 121-127, 1942. Unruh, C. C., and Kenyon, W. O.: Investigation of the Properties of Cellulose Oxidized by Nitrogen Dioxide, ibid. **64**: 127-131, 1942.

7. Frantz, V. K.: Absorbable Cotton, Paper and Gauze (Oxidized Cellulose), Ann. Surg. **118**: 116-126, 1943.

8. Putnam, T. J.: The Use of Thrombin on Soluble Cellulose in Neurosurgery, Ann. Surg. **118**: 127-129, 1943.

thrombin in 169 operations. The tissue reactions were not altered by the use of sulfadiazine or penicillin at the same time as the fibrin foam.

Because muscle has been successfully used for over thirty years as an absorbable hemostatic agent, it seemed worth while to compare the tissue reactions due to

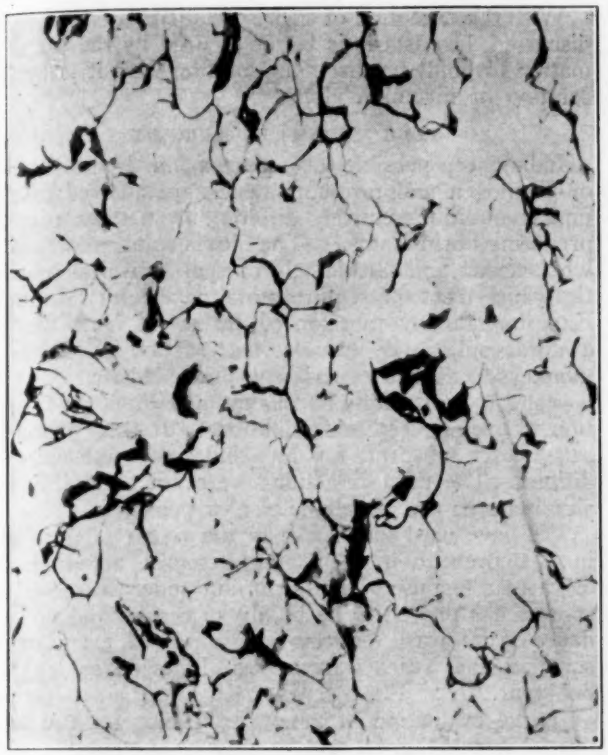

Fig. 3.—The microscopic appearance of fibrin foam.

muscle and those due to fibrin foam with thrombin. The experimental study of these two materials in the same monkey show conclusively that the tissue reaction to fibrin foam is very much less than that to muscle.[5] A large mass of fibrin foam does not excite as much tissue response as one black silk suture or a bit of bone wax.

These studies indicate that the use of fibrin foam with thrombin as an absorbable hemostatic agent is safe from the standpoint of tissue reaction, even when large amounts are required.

FIBRIN FOAM WITH THROMBIN IN GENERAL SURGERY

After fibrin foam with thrombin had been given a thorough clinical trial in neurosurgery and shown to be safe by experimental and follow-up studies, possible applications in general surgery were considered. Preliminary experimentation in various sites was therefore carried out. This indicated that the tissue reactions in the liver, peritoneum, lung, kidney and abdominal wall were similar qualitatively and quantitatively to those already described in the tissues of the central nervous system. Again it appeared that large amounts of fibrin foam with thrombin were rapidly absorbed and produced so little fibrous tissue reaction that its site could be determined with difficulty or not at all when microscopic sections were studied a month or less after operation. The use of fibrin foam with thrombin as a hemostatic agent in many sites outside the nervous system was therefore considered a safe procedure.

In neurosurgery a small amount of ooze may make the difference between success of the operation and fatality. The same amount of hemorrhage in the operative fields of the general surgeon may lead to complications in wound healing but is seldom crucial in the survival of the patient. Fibrin foam with thrombin is not therefore necessary as a routine in these procedures.

There are, however, several circumstances in which large amounts of oozing occur in general surgery and in which ligature, endothermy and other conventional methods of hemostasis are inadequate. Experience with the use of fibrin foam with thrombin in these operations has as yet been limited, but the results to date indicate that it may be possible to control the hemorrhage satisfactorily with the new absorbable hemostatic agent.

One situation in which fibrin foam with thrombin has proved valuable is the cut surface of the liver. It was possible to stop the ooze from this site when it was exposed during the resection of a large carcinoma of the stomach with extension to the right lobe of the liver. Injuries to the liver might be treated in the same way. It appears that the best way to handle hemorrhage from the cut surface of the liver is to put silver clips on spurting arteries and to coat the surface with fibrin foam soaked in thrombin. The same hemostatic agent has proved of great value in controlling ooze of the gallbladder bed in cholecystectomy. While this bleeding is satisfactorily controlled by conventional methods, the completeness and rapidity of hemostasis secured by fibrin foam with thrombin facilitates the procedure considerably.

The material also controls very well the oozing in abdominal wounds when operations are performed on jaundiced patients. It is possible to cover the entire surface of the wound with this hemostatic agent, if necessary, without fear of untoward tissue reactions.

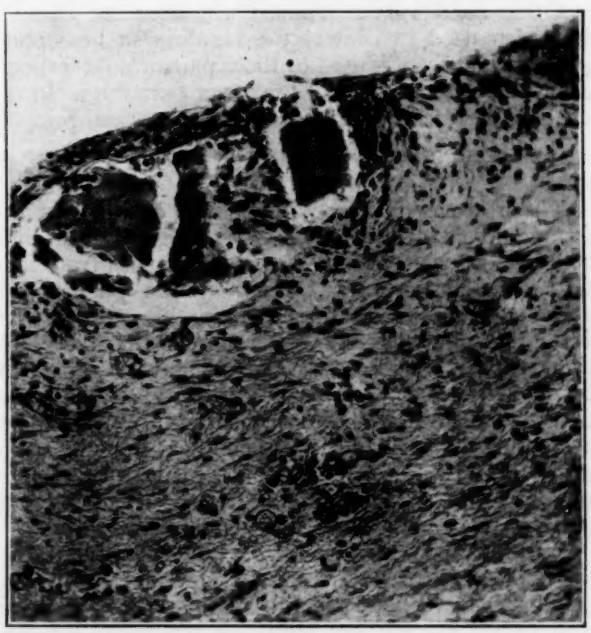

Fig. 4.—The only residuums of the large mass of fibrin foam left on the surface of the dura seventeen days previously.

Persistent ooze not controlled by the usual methods of hemostasis occurs in occasional operations undertaken for a variety of conditions. Such bleeding has responded favorably to the application of fibrin foam and thrombin in seven gynecologic procedures, as well as in radical mastectomy and nephrotomy. While on a

priori grounds it would appear that fibrin foam with thrombin would be useful in many of the operations of thoracic surgery, experience thus far has been limited. One instance is of especial interest. In this case a mediastinal tumor was resected, leaving a slowly oozing bed. Application of fibrin foam with thrombin brought the bleeding promptly and completely under control.

Further clinical experience in the use of fibrin foam with thrombin as a hemostatic agent in general surgery is accumulating rapidly. Its effectiveness in a large variety of sites has been clearly demonstrated, and no contraindications to its use have thus far appeared.

FIBRIN FOAM WITH THROMBIN IN HEMOPHILIA

The prevention of hemorrhage in hemophilia has not yet been accomplished, despite numerous investigations in that direction. Surgeons faced with operations on patients suffering from that disease are confronted with a difficult problem in deciding whether it is more dangerous to forego operation or to chance the excessive bleeding which will inevitably result. This perhaps comes up more often with tooth extractions than in any other single type of procedure. When teeth are removed from patients with hemophilia, bleeding may continue for days or weeks despite packing and transfusions. It has been shown[9] that rabbit thrombin controls such bleeding satisfactorily. Fibrin foam with thrombin has also proved to control the bleeding from the tooth sockets of patients with hemophilia quickly and completely, even when careful packing and repeated transfusions have proved ineffective.

There is considerable oozing from the tooth sockets of patients who do not have hemophilia. The packing of these tooth sockets with fibrin foam soaked in thrombin has proved of considerable value even though the serious results encountered in hemophilia were not anticipated.

Other operations in which fibrin foam and thrombin has been used to control the bleeding in hemophiliac patients has been limited to the repair of a laceration of the tongue and another of the lower extremity. In each of these instances, hemostasis was prompt and complete.

SOLUTIONS OF FIBRINOGEN AND THROMBIN IN SURGERY

There are certain conditions in which it has been found advantageous to use fibrinogen and thrombin solutions rather than products manufactured from them. Cronkite, Lozner and Deaver[10] have published an account of the use of these solutions in skin grafting. Experience in this clinic also indicates that these solutions are of considerable value in affixing skin grafts to the recipient sites. The grafts are placed in a solution of thrombin and the recipient site is painted with a solution of fibrinogen. When the thrombin soaked graft is laid on the prepared recipient site, a clot is rapidly formed. This acts as a glue which holds the graft in place and allows satisfactory taking.

Solutions of thrombin have also been used in otolaryngologic procedures. They are effective in controlling nasal hemorrhages in patients with leukemia as well as in those without blood diseases. The solutions may be painted or sprayed on the surface or applied by packing the nose with cotton soaked in thrombin. Solutions of thrombin are also of considerable value in securing hemostasis during tonsillectomy. While it would be advantageous from certain points of view to use fibrin foam soaked in thrombin under these circumstances, the possibility of aspiration of bits of foam makes one hesitate to employ it except for patients who are fully conscious and have an active gag reflex or for patients under general anesthesia who are very carefully watched.

With the exception of such special situations as those discussed, hemostasis is better secured by the use of a matrix to hold the thrombin solution than it is by the solution of thrombin alone.

FIBRIN FILM IN SURGERY

It has been possible to prepare a film from solutions of fibrinogen and thrombin which are allowed to clot under conditions entirely different from those used in preparing fibrin foams.[11] The film is translucent, somewhat elastic and pliable. It presents physical properties which meet the requirements for a dural substitute. Experimental investigation of the use of fibrin film as a dural substitute was carried out on a series of monkeys.[12] These experiments indicated that the film was slowly replaced by fibrous tissue without the formation of meningocerebral adhesions. It thus proved a satisfactory substitute for dura under experimental conditions. The tissue reactions were not altered by the simultaneous use of sulfadiazine or penicillin.

We have used fibrin film in the repair of dura and in the prevention of meningocerebral adhesions in 59 cases. The use of the fibrin film under these circumstances has proved to be highly successful and no evidence of untoward sequelae have appeared, even though some of the patients have been followed as long as one year.

In the evaluation of a new substance for use as a dural substitute, great caution must be exercised because of the possibility of the late appearance of unfavorable reactions to its presence. In our experience so far, fibrin film has proved more satisfactory than any other material tested as a dural substitute. In addition to its safety, fibrin film is well adapted for use in the repair of dural defects because of its translucence, flexibility, ease of handling and adaptability to any contour.

It is possible that there may be applications of fibrin film to problems in general surgery. To this end, experiments have been begun to test the tissue reactions of fibrin films in joints, in the eye, in the peritoneum, about nerves and elsewhere. These applications of fibrin film are at present in the experimental stage, and the use of the material except as a dural substitute is not recommended at this time. The possibility of unfavorable reaction to fibrin film in general surgery must be borne in mind and each site thoroughly investigated experimentally before it is used in the clinic.

SUMMARY

The preparation of purified human fibrinogen and thrombin has made possible new materials for use in surgery. The solutions of the proteins may be employed and a variety of products prepared by combining them under different conditions.

Of these, fibrin foam with thrombin is a new absorbable hemostatic agent prepared from fibrinogen and thrombin of human blood plasma.

9. Lozner, E. L.; MacDonald, H.; Finland, H., and Taylor, F. H. L.: The Use of Rabbit Thrombin as a Local Hemostatic, Am. J. M. Sc. **202**: 593-598, 1941.

10. Cronkite, E. P.; Lozner, E. L., and Deaver, J. M.: Use of Thrombin and Fibrinogen in Skin Grafting, J. A. M. A. **124**: 976-978 (April 1) 1944.

11. Ferry, J. D., and Morrison, P. R.: Chemical, Clinical and Immunological Studies on the Products of Human Plasma Fractionation; XVII. Fibrin Clots, Fibrin Films, and Fibrinogen Plastics, J. Clin. Investigation **23**: 566-572, 1944.

12. Bailey, O. T., and Ingraham, F. D.: Chemical, Clinical and Immunological Studies on the Products of Human Plasma Fractionation: XXII. Fibrin Films in Neurosurgery with Special Reference to Their Use in the Repair of Dural Defects and in the Prevention of Meningocerebral Adhesions, J. Clin. Investigation **23**: 597-600, 1944. Bailey and Ingraham.[2]

Extensive clinical use of fibrin foam with thrombin in neurosurgical operations has shown it to control oozing from the dura, from beneath bone flaps and from the cerebral tissues as well as from the dural sinuses and large veins. It is not recommended for brisk arterial hemorrhage.

The tissue reaction to fibrin foam with thrombin is minimal and negligible from the clinical standpoint. In this respect, as well as in availability, ease of manipulation and adaptability, it is much superior to muscle. Fibrin foam with thrombin is prepared wholly from materials of human origin.

This hemostatic agent can be used with advantage in certain procedures by the general surgeon. It is also effective in controlling hemorrhage in patients with hemophilia.

A limited use has been made of solutions of fibrinogen and thrombin in certain special situations in which it is desirable to form a clot in situ.

Fibrin film is a homogeneous sheet prepared from human fibrinogen and thrombin. It has proved effective in the repair of dural defects and in the prevention of meningocerebral adhesions.

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ABSTRACT OF DISCUSSION

ON PAPERS OF DR. JANEWAY AND DRS. INGRAHAM AND BAILEY

DR. ORVILLE T. BAILEY, Boston: There has been an inclination, because of the nature of most investigations on purified proteins, to regard them as unstable substances, but the preparations of albumin may be frozen, thawed and injected clinically without causing reactions. They may be kept at tropical temperatures for periods of many months, and severe shaking does not change them in such a way that they cause reactions in patients when injected subsequently. A number of hospitals have sent the tissues of patients receiving large amounts of albumin to learn whether there are any pathologic effects which may be due to the presence of the administration of such an unusual amount of one fraction of human plasma. Pathologic changes which could be correlated with the injection of the albumin could not be found. Since fibrin foam, to be effective, must be left in place, it should elicit a minimal tissue reaction and this is found to be the case. Fibrin foam, when it is fixed directly, consists of cross sections of the honeycombs of which it is composed. When it has been left on the surface of the dura for fourteen hours the meshes of the honeycomb have become filled with blood clot. There is practically no cellular infiltration in response to its presence. At the end of twenty-four days a large mass of fibrin foam has become reduced to a small structure, filling only a high power field, and is surrounded by a minimal amount of connective tissue. It is difficult to make sure that even this small amount of connective tissue is due wholly to the presence of the fibrin foam, because the blood clot which the fibrin foam is left in place to produce will usually result in the production of more fibrous tissue than that. Experiments were set up in monkeys to compare the tissue reaction of muscle and fibrin foam as hemostatic agents. The material was introduced into the cerebral cortex. At the end of four weeks there is practically no reaction to the presence of the fibrin foam. It has become somewhat coalesced and is nearly absorbed. When a piece of muscle of similar size is left in a comparable place on the opposite side of the same animal there is considerable gliosis about the fragment, and the muscle is being converted into a mass of richly collagenous connective tissue. Some of the blood vessels which were present in the original fragment of the muscle are still present. This indicates that the reaction to fibrin foam is many times less than it is to muscle, and this permits us to use fibrin foam in a great many situations where we might fear tissue reaction from muscle.

A STUDY OF "PENICILLIN FAILURES"

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AND
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SAN FRANCISCO

In studying a new therapeutic agent it is neccessary not only to discover the conditions in which it is effective but also to define the circumstances under which it fails or at least yields unsatisfactory results. Penicillin has now been used long enough to make possible the compilation of lists of those infections in which it seems to be of value.[1] But such bare enumerations do not begin to tell the story, as there are all sorts of special circumstances which arise in the individual case to modify any general statement. From an intensive study of over 100 patients treated with penicillin a good deal has been learned about what might be called "penicillin failures"; it is with this phase of the subject that the present paper is concerned.

"Penicillin failures" may be discussed under the following headings:

1. Causes of death in penicillin treated patients.
2. Failures due to inadequate amounts of penicillin.
3. Failures due to inadequate surgical drainage in penicillin treated cases.
4. Failures due to overwhelming infection even when penicillin dosage was presumably adequate.
5. Failure to prevent or cure renal lesions in penicillin treated cases of streptococcic infection.
6. Conditions in which penicillin either fails or is likely to be inadequate.

1. CAUSES OF DEATH IN PENICILLIN TREATED CASES

Aside from patients who were not seriously ill, such as those with primary syphilis, mild sulfonamide fast gonorrhea or furunculosis, we have treated 87 instances of severe infection including endocarditis, meningitis and acute osteomyelitis. An idea of the general character of the material is obtained from the fact that 27, or 31 per cent, of these patients had bacteremia. Of this series of 87 patients 7, or 8 per cent, died. An analysis of these fatal cases is given in the accompanying table. It appears that only 2 deaths (cases 6 and 7), or 2.3 per cent of the whole series, could be ascribed to actual failure of penicillin treatment. Ten years ago one would have had a mortality of at least 50 per cent.

2. FAILURES DUE TO INSUFFICIENT PENICILLIN THERAPY

It is not our present purpose to discuss the unsettled question of adequate penicillin dosage. Excellent results have been reported with relatively small quantities of the material,[2] but this does not rule out the need of larger doses in some cases. At any rate the unsatisfactory results in the following patients seemed to be ascribable to too small amounts of penicillin or to treatment of too brief duration.

From the Department of Medicine, Stanford University School of Medicine.

The Penicillin was provided by the Office of Scientific Research and Development from supplies assigned by the Committee on Medical Research for clinical investigations recommended by the Committee on Chemotherapeutics and Other Agents of the National Research Council.

1. Memorandum of Office of Civilian Penicillin Distribution, Chicago, May 1944.
2. Herrell, W. E.: The Clinical Use of Penicillin, an Antibacterial Agent of Biologic Origin, J. A. M. A. **124**: 622 (March 4) 1944.

The following case concerns relapse of an infection which probably could have been prevented by more prolonged treatment of the original attack, although the daily dose seemed adequate:

CASE 8.—A woman aged 61 entered the hospital on the fifth day of a typical facial erysipelas. The eruption extended over the nose to the malar prominences and ordinarily would have continued to spread for several days. She was given an intravenous dose of 35,000 units of penicillin and thereafter 15,000 units intramuscularly every three hours. There was no further spread of the process, and within twenty-four hours it seemed to have completely subsided. The temperature dropped promptly (fig. 1) and penicillin was continued for only two days—a total of 255,000 units. Three days later she left the hospital apparently well but after an interval of seven days returned again with typical facial erysipelas. This was clearly a second attack and not a residue of the first. Penicillin was given once more with prompt arrest of the erysipelas, but this time treatment was continued for nine days—a total of 1,180,000 units (fig. 1).

There is every reason to believe that the second attack would not have occurred had treatment been continued for a longer time after the first bout. It seems clear that with any serious infection it may be well to continue treatment for several days after the process has been controlled as possible insurance against recurrence. This applies especially to staphylococcic and streptococcic infections. In Streptococcus viridans subacute bacterial endocarditis the good results which we have obtained in a consecutive series of 9 cases seems due to the continuation of uninterrupted treatment over a period of six to eight weeks. Recurrences of acute hemolytic streptococcus throat infections, common with brief treatment,[3] can be prevented by giving penicillin over a period of five to ten days.

Patients Who Died Under Penicillin Treatment

Case	Clinical Diagnosis	Treatment	Anatomic Diagnosis	Comment
1	Lung abscess following aspiration of potato chip, 4 weeks' duration; high fever; abscess at least 15 cm. in diameter; huge amount of foul sputum containing various streptococci and putrefactive anaerobes; a desperately ill patient with progressive gangrene of lung, with diabetes of moderate severity	Penicillin by continuous intravenous drip, 300,000 units per day; after 3 days with condition generally better she died suddenly in acute collapse	A huge lung abscess occupying practically the entire right upper lobe was found; there was no evidence of air embolus, no pulmonary embolus, no edema of lungs; in short, no anatomic cause of death was found	Contents of abscess obtained at autopsy showed no growth on culture, so that the penicillin had been effective to some extent; treatment had not gone on long enough before she died to draw any further conclusions as to efficacy; no cause for sudden death was found; the lots of penicillin used in this case gave no reactions in other patients, and penicillin clearly had nothing to do with her death
2	A patient in the last stages of lymphoid leukemia developed acute lobar pneumonia of left lung with 150 colonies per cubic centimeter of type 1 pneumococcus	Treatment started on fifth day of disease, 200,000 to 300,000 units by continuous intravenous drip; rapid improvement and 12 days later when apparently convalescent went into collapse with high fever and died in 24 hours	The pneumonia on the left was practically resolved; there was a fresh consolidation of the right middle lobe, which showed no pneumococci but an unidentified bacillus; extensive lesions of leukemia	A dying leukemic woman with terminal type 1 pneumococcic sepsis with heavy bacteremia and lung consolidation was cleared of her pneumococcic infection but died of leukemia and another different (bacillary) infection
3	A young man with a fistula from esophagus to lung and huge paravertebral abscesses from which nonhemolytic streptococci (sensitive to penicillin) were grown; no tubercle bacilli found on extensive search of pus and sputum	Intensive intravenous, intramuscular and local penicillin therapy for about a month	Huge tuberculous paravertebral abscesses; tubercle bacilli easily demonstrated in scrapings from granulation tissue	A misdiagnosis. This patient would not have been treated had the correct diagnosis of tuberculosis been made
4	A man aged 46 had pneumococcic sepsis with 25 to 50 colonies of type 25 pneumococcus per cubic centimeter of blood; there were evidences of endocarditis, arthritis and meningitis	Intensive treatment of up to 400,000 units daily by intravenous drip, also intrathecal penicillin; treatment over a period of 3 weeks eliminated all evidence of pneumococcic infection (sterile blood and spinal fluid cultures) but he developed a huge bed sore with general failure and died	No autopsy.....	There was every evidence here that the pneumococcic sepsis was cured; death was clearly due to infection from a huge bed sore and perhaps could have been avoided
5	A woman aged 22 was desperately ill with a gas bacillus infection following attempted abortion (Clostridium welchi grown from cervical discharge)	After 5 days of intensive penicillin therapy by intravenous drip the gas bacillus infection was entirely cleared; she was oliguric on entry and went on to uremia and anuria of obscure origin—possibly associated with transfusion or sulfonamides received before entry	All evidences of uterine infection cleared up; kidneys showed a peculiar diffuse lesion—still under study	C. welchi infection cleared under penicillin, but she died of renal disease which was already under way when treatment was started
6	A woman aged 39 with old rheumatic mitral disease infected her finger by pin prick and developed Staph. aureus bacteremia, 800 colonies per cubic centimeter; she seemed moribund with jaundice, high fever and anemia; the staphylococcus was highly sensitive to penicillin in test tube	Given penicillin by intravenous drip at rate of 300,000 units in first 20 hours; at this time blood culture (with penicillinase) still positive—130 colonies per cubic centimeter—no growth without penicillinase, indicating a high blood level; progressive cyanosis and dyspnea; death 24 hours after entry	Old mitral lesion with fresh acute ulcerative endocarditis; no special cause of death found	This case must be considered a penicillin failure; in spite of intensive treatment and high blood level, bacteremia was not controlled soon enough and she died in toxemia
7	A man aged 59 was in hospital for nearly 5 months with recurring S. aureus sepsis	Received a total of 7,500,000 units of penicillin	Subacute pericarditis, subacute meningitis, small abscesses in kidney	This case also must be set down as penicillin failure, although it is now believed that his treatment was inadequate in amount

In the next case also the poor result may be due to the fact that treatment was stopped too soon:

CASE 9.—A school boy aged 8 years was admitted on the third day of an acute osteomyelitis of the left femur. The left thigh was hot, red, greatly swollen and acutely painful. There was high fever with leukocytosis, and a blood culture was positive for S. aureus. Penicillin was started on the following (fourth) day in doses of 150,000 units per day by continuous intravenous drip. Treatment was continued for only twelve days and was then stopped, although the temperature

3. Rantz, L. A.: Personal communication to the authors.

had not yet reached normal (fig. 2). A roentgenogram on entry showed no visible lesion in the bone, but on the thirteenth day of the disease an early destructive process was detected by x-ray just proximal to the epiphysial line of the lower femur. No periosteal reaction was seen at this time. The patient left the hospital on the twenty-fourth day of the disease

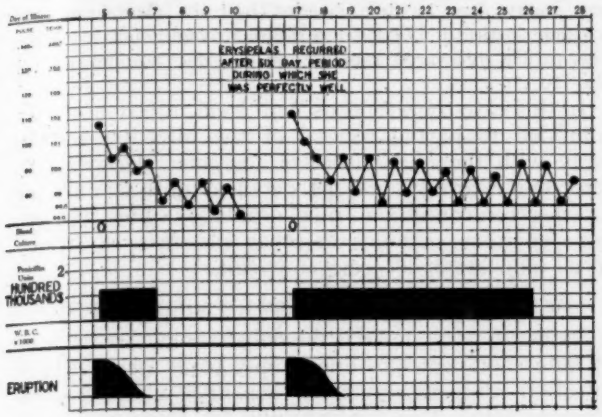

Fig. 1.—Graphic record of case 8.

with normal temperature, no pain and only very slight swelling of the leg just above the left knee. Frequent roentgenograms from this time on showed progressive destruction and absorption of the lower two thirds of the femur and a pronounced periosteal reaction throughout its length. After three months there was obvious sequestration and finally a pathologic fracture. X-ray films made on the thirteenth day and at the height of the lesion several months later are shown in figures 3 and 4.

Our experience in 8 cases of acute osteomyelitis of the long bones in which no operation was done indicates that very intensive and prolonged therapy is necessary if serious changes are to be prevented. Even then, as reported by others also, the x-rays from the second week on usually show some absorption of cortex with periosteal reaction possibly due to injury which began before penicillin therapy was started. Some staphylococci must be sealed in and difficult to reach in areas made relatively avascular by thrombosis and necrosis. It is possible, if not probable, that more prolonged therapy of patient 9 might have arrested the process at an earlier stage as it appears to have done

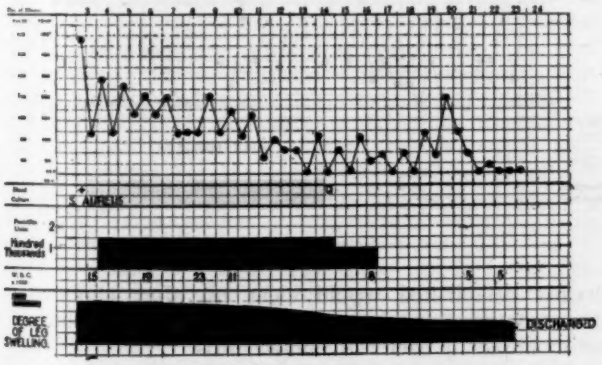

Fig. 2.—Graphic record of case 9.

in our other cases. At any rate prolonged uninterrupted treatment is clearly indicated in acute osteomyelitis. This whole subject will be dealt with in detail in another paper.

In case 7 in the table it is our belief that death might have been prevented by more intensive and continuous therapy.

This man, with severe diabetes, developed S. aureus sepsis with positive blood culture following a skin injury. On entry there were skin lesions and osteomyelitis of the left humerus. Pericarditis was detected (friction rub) a few days later. He was one of our early cases and after ten days of penicillin (2,000,000 units) treatment was arbitrarily stopped. Over a period of five months there were repeated episodes of S. aureus infection of various structures with recurring positive blood culture, although the organism was always sensitive to penicillin in vitro. Treatment with penicillin, given during each exacerbation, in the end totaled 7,500,000 units but was never continued over a period of more than ten days at a time. The patient finally left the hospital feeling fairly well, with normal temperature and with no obvious foci, but on reaching home he again developed fever with left upper abdominal pain, failed rapidly and died in twelve days. At autopsy pertinent points were "subacute and chronic pericarditis, subacute and chronic myocarditis, subacute meningitis, small abscesses of kidney." There were also large infarcts of the spleen.

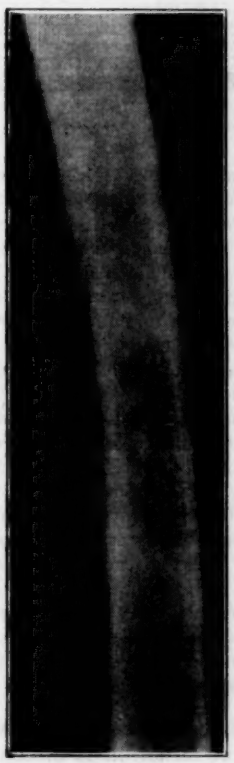

Fig. 3.—Left femur in case 9 on December 20, the thirteenth day of disease, showing early absorption and periostitis.

Fig. 4.—left femur in case 9 on April 4, showing advanced changes with sequestration and pathologic fracture.

This patient furnishes a typical example of penicillin therapy which during a long relapsing infection always fell short of the mark. It seems probable from experience in subsequent cases that intensive uninterrupted treatment over a period of four to six weeks would have cured this man. The hazard of too little and too brief therapy, which in our experience is especially great with staphylococcic infections, is illustrated.

3. FAILURES ASSOCIATED WITH PENICILLIN THERAPY WHEN ADEQUATE SURGICAL DRAINAGE OF INFECTIONS WAS NOT CARRIED OUT

In spite of the great efficacy of penicillin in controlling certain types of infection, the principle that evacuation of closed collections of pus is necessary for rapid cure still holds good in most cases.[4] Simple

4. Keefer, C. S., and others: Penicillin in the Treatment of Infections, J. A. M. A. **122**: 1217 (Aug. 28) 1943.

aspiration of pneumococcic empyema [5] and of gonococcic joints, with injection of penicillin, has, to be sure, been adequate in many cases, but with other infections, especially those due to staphylococci and nonhemolytic streptococci, progress may be arrested until surgical drainage has been instituted. The problem is illustrated by the following cases:

CASE 10.—A man aged 38 developed subphrenic abscesses probably following perforation of a viscus. The abscesses were incised and drained and an anaerobic nonhemolytic streptococcus, highly sensitive to penicillin, was isolated. He received intensive penicilin therapy (2,290,000 units) by continuous intravenous drip, as well as locally, for eleven days. His temperature gradually fell almost to normal and he seemed much better, but fever recurred with leukocytosis and abdominal pain. It was evident that there was more pus, and drainage of an encapsulated pocket was done through the previous incision. Penicillin (1,515,000 units) was given intramuscularly over a period of eleven days and the temperature again fell to normal with clinical improvement. He was not entirely well, however, and fever soon returned. This time x-rays showed a lung abscess which appeared to have developed under penicillin therapy. The same organism obtained from the subphrenic abscess was grown from the lung lesion, which was drained surgically. Another intramuscular course of 1,000,000 units was given with injection of 26,000 units into the abscess cavity. There was now rapid healing of all lesions, and the patient was discharged well after a hospital stay of three months and a total of 7,400,00 units of penicillin. Figure 5 shows the portions of the course before and after drainage of the lung abscess. One sees that in spite of intensive penicillin the temperature did not drop until drainage was instituted.

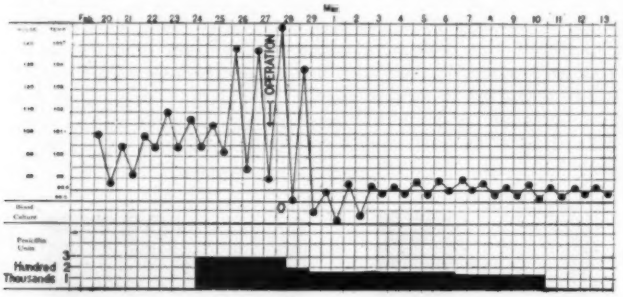

Fig. 5.—Graphic record of case 10.

The streptococcus in this case was highly sensitive to penicillin in vitro, but the whole situation is difficult to evaluate. Those who saw him felt that he did better than patients of this sort usually do with surgery alone. On the other hand there were two relapses in spite of intensive penicillin treatment, each associated with an undrained collection of pus.

The following case is even more clearcut:

CASE 11.—A man aged 66 was brought to the hospital with the story of sudden onset of sharp pain in the right side of the chest two weeks previously. This had continued with fever, prostration and general failure. There had not been cough, sputum or any suggestion of bronchitis or pneumonia. On entry he looked ill and had sweats and fever. There were signs of fluid in the right chest and, on tapping, thin yellow purulent fluid was obtained. It had an extremely foul odor. Smears showed innumerable bacteria and on culture nonhemolytic streptococci and an unidentified gram positive bacillus were grown. Between April 13 and April 29 the chest was aspirated seven times, and on five occasions penicillin was injected into the pleural cavity in amounts of 50,000 to 100,000 units, a total of 495,000 units. There was considerable improvement under this program, and by the 29th the fluid was no longer foul and no organisms were seen or grown. However, 50 cc. of yellow thickish pus was obtained and the patient continued to feel ill and to have a variable fever with leukocytosis. On April 27 (fig. 6) penicillin was started intramuscularly at the rate of 120,000 units daily in eight doses, but after five days there was no improvement so that operation was finally done, a tube inserted into the pleura and tidal drainage instituted. The temperature promptly fell to normal. The patient recovered rapidly and left the hospital well on May 20.

In this case thoracentesis with local injection of penicillin led to partial control of the infection and did away with the foul nature of the pus. However, no complete clearing could be obtained until a tube was inserted for continuous tidal drainage. This has been our general experience in other instances of streptococcic and staphylococcic empyema.

4. FAILURES DUE TO OVERWHELMING INFECTION

Patient 6 in the table is the only example we have had of failure of penicillin due simply to an overwhelming infection with an organism sensitive in vitro. She received large doses of penicillin by continuous intravenous drip, sufficient to raise the blood content to well over the standard bacteriostatic level of 0.15 unit per cubic centimeter.[6] In spite of this the blood stream was not cleared and after twenty hours culture still yielded 130 colonies of S. aureus per cubic centimeter. The importance of using penicillinase [7] is also brought out, as there was enough penicillin in the blood to inhibit growth in a blood culture made without penicillinase.

5. FAILURE TO PREVENT OR CURE THE DEVELOPMENT OF GLOMERULAR NEPHRITIS IN CERTAIN PATIENTS WITH STREPTOCOCCIC INFECTIONS TREATED WITH PENICILLIN

The association of glomerulonephritis with certain types of streptococcic infection is clearly established. When penicillin became available it seemed of particular importance to find out if this agent, which extirpates so many streptococcic infections with great speed, would prevent the occurrence of nephritis. Of no less interest was the question of whether nephritis already established would clear up after elimination of concomitant streptococcic infection by penicillin, as for example in bacterial endocarditis.

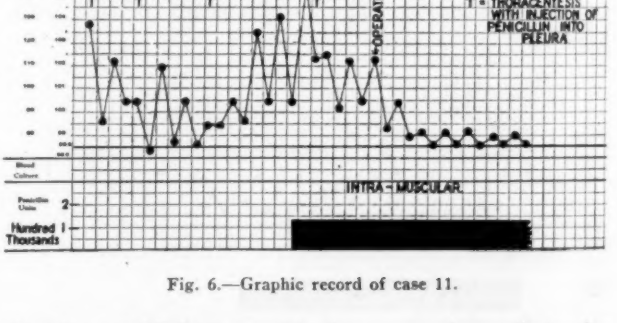

Fig. 6.—Graphic record of case 11.

CASE 12.—A man aged 66, some time after a burn of the left shoulder, was brought to another hospital because of high fever, shortness of breath and swelling of the left leg. Blood culture was found positive for hemolytic streptococci but in spite of intensive sulfadiazine therapy and two transfusions

5. Tillett, W. S.; Camber, M. J., and McCormack, J. E.: The Treatment of Lobar Pneumonia and Pneumococcal Empyema with Penicillin, Bull. New York Acad. Med. **20**: 142, 1944.

6. Rammelkamp, C. H., and Keefer, C. S.: Penicillin: Its Antibacterial Effect in Whole Blood and Serum for the Hemolytic Streptococcus and Staphylococcus Aureus, J. Clin. Investigation **22**: 649, 1943.

7. Kirby, W. M. M.: Extraction of a Highly Potent Penicillin Inactivator from Penicillin Resistant Staphylococci, Science **99**: 452, 1944.

he had gone steadily downhill. On entry to Stanford Hospital (fig. 7) he seemed desperately ill. The temperature was 40.5 C. (104.9 F.). The remains of a small burn on the right shoulder were visible but the lesion was almost healed. There were many petechiae, a faint systolic murmur at the apex and soft edema of both ankles, but the left leg was much more swollen than the right. Blood culture yielded 400 colonies per cubic centimeter of hemolytic streptococci. He was moderately anemic and the blood urea was 90 mg. per hundred cubic centimeters. The urine contained considerable protein, immense numbers of red cells, white cells and casts of all sorts. The

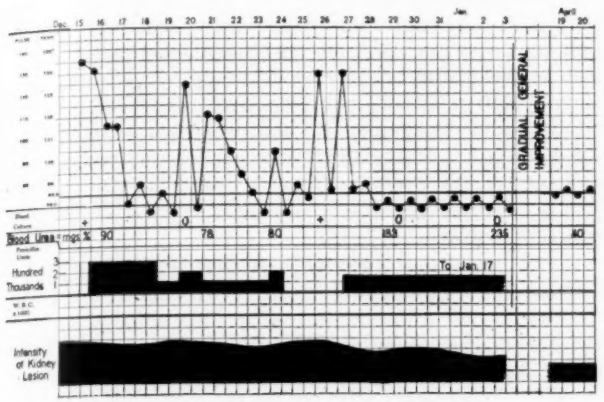

Fig. 7.—Graphic record of case 12.

diagnosis was sepsis, hemolytic streptococcus, with bacteremia, phlebitis of the left femoral vein, and acute glomerular nephritis associated with the streptococcic infection. Penicillin was given by continuous intravenous drip at the rate of 300,000 units per day, and within twenty-four hours the blood culture showed no growth and the temperature fell abruptly to normal. On the fifth day there was an unexplained rise of temperature, which may have been due to a small pulmonary embolus. Penicillin was stopped on the ninth day with the temperature normal and the patient much improved, but the urine was essentially unchanged and the blood urea was still 78 mg. per hundred cubic centimeters. Two days after penicillin was stopped he had a chill with rise of temperature to 40 C. (104 F.) and blood culture was again positive, showing 5 colonies of hemolytic streptococci per cubic centimeter. Penicillin was given again, intramuscularly, for three weeks. The temperature fell promptly to normal and never rose again above 37.5 C. (99.5 F.) nor was the blood culture again positive.

In spite of the elimination of the streptococcic infection the nephritis seemed unaffected. The urine continued to show protein, large numbers of red cells and casts. The blood urea rose as high as 235 mg. per hundred cubic centimeters. Soft edema continued. His general condition gradually improved, so that by May 1944, four months after leaving the hospital, he felt very well and the blood urea was only 40 mg. per hundred cubic centimeters. The blood pressure was 150/85. Except for slight pitting, edema had disappeared. The urine, however, showed the typical findings of a glomerular nephritis in the subacute stage. An Addis count gave protein 0.35 Gm. in twenty-four hours, red blood cells 250 million in twenty-four hours, white and epithelial cells 55 million in twenty-four hours and casts 500,000 (granular, hyaline and a few blood casts). This case also illustrates relapse of an acute infection with recurrence of positive blood culture when penicillin was stopped too soon.

There is every reason to believe that this patient's streptococcic infection was completely eliminated. There is no evidence, however, that the course of the nephritis was influenced and every reason to believe that an irreversible lesion has been set up which will progress in the usual relentless fashion of chronic glomerulonephritis.

Similar observations by one of us (C. D. A.) in cases of S. viridans bacterial endocarditis have shown that the renal lesion may persist after the infection has been eliminated. All this is in harmony with the evidence accumulated by Addis [8] to the effect that glomerular nephritis, once under way, tends to propagate itself.

6. CONDITIONS IN WHICH PENICILLIN EITHER FAILS OR IS LIKELY TO BE INADEQUATE

Pneumococcic Meningitis. — Although pneumococci are often highly sensitive to penicillin, the results of treatment of pneumococcic meningitis have in our hands been unsatisfactory in many ways. These poor results are doubtless attributable in some degree to the nature of this infection [9] with its well known tendency to adhesive arachnoiditis, encephalitis and thick gelatinous exudate, which impedes the local application of any therapeutic agent. Three patients with pneumococcic meningitis, probably of otitic origin, all survived their infection after intensive penicillin treatment given intrathecally, by injection into the ventricles and by intramuscular or intravenous injection, but in each instance serious neuropsychiatric residues reduced them to an essentially vegetative state. The following case is typical:

CASE 13.—A man aged 48, a gardener, was found comatose in his home two days before entry. He had previously been well. He was found to have signs of meningitis, and type 12 pneumococcus was grown from the blood and spinal fluid. He failed to improve on intravenous sulfadiazine and antipneumococcus serum and was sent into Stanford Hospital for penicillin. He was flushed, restless and delirious. The neck was stiff. There was some pus in the left auditory meatus but there were no signs of mastoiditis. He was started on large doses of penicillin by continuous intravenous drip, later changing to the intramuscular route (200,000 units per day). He also received 10,000 units in 10 cc. of saline solution intraspinally almost daily for the first eight days. On the ninth day, as he had not improved, the ventricles were tapped but there was no evidence of block. His temperature gradually subsided over twenty-six days, but the spinal fluid still showed cells and protein. After eleven days there was a relapse with slight fever and considerable disorientation, but pneumococci were not recovered from the spinal fluid. However, he was given more penicillin intramuscularly and four intrathecal injections of 5,000 units each. He remained mildly confused and had a peculiar visual difficulty characterized by ability to see objects but difficulty in naming them. He could read words aloud but could not read consecutively or understand what he read. At the time he left the hospital, two months after entry, the spinal fluid still showed increased cells and protein suggestive of arachnoiditis, but he was much improved. The temperature was normal. He was oriented and talked rationally for the most part. There was still a pronounced personality change with general mild mental deterioration. Six weeks after leaving the hospital there was not much change.

Poor results in this small series of cases should not be taken as a final evaluation of penicillin in pneumococcic infections and better results have been reported by others.[10] However, our cases were treated intensively, both intrathecally, by ventricular puncture and by the intravenous and intramuscular routes and it seems unlikely that the outcome was due to too little treatment. Since sulfonamides are quite effective in pneumococcic meningitis, it may turn out that sulfonamides together with penicillin may be the best treatment for this condi-

8. Addis, T.: Unpublished observations.
9. Ruegsegger, J. M.: Pneumococcal Meningitis, Ann. Int. Med. **17**: 693, 1942.
10. Dawson, M. H., and Hobby, G. L.: The Clinical Use of Penicillin: Observations in 100 Cases, J. A. M. A. **124**: 611 (March 4) 1944.

tion. It seems especially important that some of our cases did not come under treatment until late in the disease. In the long run better results will undoubtedly be obtained if penicillin therapy is started on the first or second day of the meningitis.

Chronic (Staphylococcic) Osteomyelitis.—In contrast to acute staphylococcic osteomyelitis our results in most of the chronic cases have been unsatisfactory. If the lesion is in a long bone and can be laid wide open by surgical means, local penicillin irrigations seem to aid in rapid healing. In cases with sinuses leading into the pelvic bones or into the spine and inaccessible to surgery, neither local irrigations nor heavy intramuscular injections have had any definite effect in our hands.

CONDITIONS IN WHICH PENICILLIN WAS ENTIRELY INEFFECTIVE

During the course of our work penicillin was used in infections occurring along with other diseases, thus giving an opportunity to evaluate the material in conditions in which it ordinarily would not be used. The results agree with those obtained by others [1] but may be enumerated:

Tuberculous paravertebral abscess, no effect.
Lymphoid leukemia, no effect.
Aleukemic myeloid leukemia, no effect.
Infectious mononucleosis, no effect. (This condition developed in a patient with acute osteomyelitis while under active penicillin treatment.)
Mycosis fungoides, no effect.
Chronic (rheumatoid) arthritis, no effect.
Filariasis, no effect. (Blood count of microfilariae remained unchanged during penicillin administration.)

RELATION OF PENICILLIN FAILURE TO SENSITIVITY OF STRAINS IN VITRO

Even within categories of bacteria such as streptococci, staphylococci and others which are in general sensitive to penicillin there may be strains which are resistant in vitro. It is important to know whether such strain resistance in the test tube runs parallel with resistance to therapy in disease. It has been noteworthy that practically all of our strains of pneumococci, streptococci and staphylococci recovered from clinical cases of active infection were inhibited in the general range of 0.1 unit per cubic centimeter of culture medium. The relations with staphylococci are quite complicated and are discussed in detail in other papers from this clinic;[11] most of our penicillin resistant strains of this organism were recovered from sources other than active infections. There are strong suggestions, however, that some correlation exists between strain sensitivity in vitro and clinical response. This is well brought out in our series of 10 cases of subacute bacterial endocarditis caused by nonhemolytic streptococci. Eight strains were highly sensitive to penicillin in vitro, and all of the patients infected with these were promptly rendered bacteria free. In 1 of them culture made only two hours after penicillin was started was negative, as were all subsequent cultures. In the ninth case a strain was obtained which required two or three times the usual concentration of penicillin to produce inhibition in the test tube and with this patient intensive (200,000 to 300,000 units per day) treatment was carried on for nineteen days before the temperature began to fall, although blood cultures were negative after penicillin was given. The strain from the tenth case was not inhibited in vitro even with very high concentrations of penicillin, and this patient failed to respond clinically to doses as high as 450,000 units per day, while blood cultures remained consistently positive.

It is evident, therefore, that failure of therapy in an individual case may be due to strain resistance, and the need of in vitro tests in routine work is emphasized.

We have not so far encountered the phenomenon of a strain becoming penicillin fast during the course of treatment, although this possibility has been raised both on experimental and on clinical grounds.[12] In a case of relapsing staphylococcic sepsis, for example, many positive blood cultures over a period of five months yielded organisms which were all equally sensitive even though treatment had been inadequate. It does not seem probable that induced penicillin fastness will turn out to be a major factor in clinical penicillin failures.

COMMENT

Penicillin failures fall under two main headings: First there are those diseases or infections which are entirely unaffected by penicillin. Those are now pretty well known and are enumerated in the memorandum [1] of the Office of Civilian Penicillin Distribution. Secondly there are the infections which in a general way are amenable to penicillin but in which special circumstances may lead to failure in the individual case. The present analysis deals with this problem.

Patients with infections by bacteria which are sensitive to the actions of penicillin may die or may relapse because of inadequate dosage. The daily amount may be too small, but the time factor is likely to be more important. This is clearly established in S. viridans bacterial endocarditis, and in hemolytic streptococcus and staphylococcus infections. A daily dose which may be adequate if given over periods of weeks or months may fail to cure if given for a few days only, even though the infection seems at first to be eliminated. We believe that the question of optimum dosage both as to frequency and as to size of daily injections and as to total duration of treatment is the most important practical problem in penicillin therapy at the present time.

The question of whether collections of pus can be disposed of by aspiration and injection of penicillin without surgical drainage is also one of great importance. In general the position seems secure that such surgical drainage will be necessary in addition to penicillin. This applies, in our experience, to empyema, lung abscess, subphrenic abscess and brain abscess, even though certain local collections caused by specially sensitive organisms (gonococci, pneumococci [5]) and located in favorable situations may be cured by aspiration and injection alone. Ordinarily if such a lesion is not cured or definitely improving after a week of injection therapy surgical drainage should be done. In some cases surgery is obviously necessary when the patient is first seen.

Penicillin may fail in infections with a highly sensitive organism even when given in huge doses. Under these circumstances either the patient is seen in a late stage of the disease or there is an overwhelming infection.

11. Rantz, L. A., and Kirby, W. M. M.: The Action of Penicillin on the Staphylococcus in Vitro, to be published. Kirby, W. M. M.: Bacteriostatic and Lytic Actions of Penicillin on Sensitive and Resistant Staphylococci, to be published.

12. McKee, C. H., and Houck, C. L.: Induced Resistance to Penicillin of Cultures of Staphylococci, Pneumococci and Streptococci, Proc. Soc. Exper. Biol. & Med. **53**: 33, 1943. Rammelkamp, C. H., and Maxon, T.: Resistance of Staphylococcus Aureus to the Action of Penicillin, ibid. **51**: 386, 1942.

In general elimination of streptococcic infections by penicillin will not be followed by healing of an associated nephritis. In certain conditions, such as pneumococcic meningitis, the nature of the lesions makes adequate application of penicillin difficult, and serious neuropsychiatric sequelae are likely to result even if the infection is overcome and the patient lives. Chronic staphylococcic osteomyelitis of the spine or pelvic bones not amenable to wide surgical exposure has in our experience not been influenced by penicillin even though the strains are sensitive in vitro.

SUMMARY

Penicillin failures for the most part fall into the following groups:

1. Cases in which the treatment is too brief or the daily dose too small.
2. Cases in which penicillin fails unless surgical drainage is also done.
3. Overwhelming infection, even with a sensitive strain.

Penicillin may fail to prevent the development or progress of nephritis even if the predisposing (streptococcic) infection is eliminated.

Penicillin treatment of pneumococcic meningitis may be followed by chronic neuropsychiatric disturbances.

There is probably a correlation between strain sensitivity in vitro and clinical amenability to penicillin therapy.

Development of penicillin fastness probably plays little part in therapeutic failures.

THE TOXIC REACTIONS OF THE NEWER SULFONAMIDES

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In the past four years 1,936 patients in the medical wards at the Cincinnati General Hospital have been treated with sulfathiazole, sulfadiazine, sulfapyrazine, sulfaguanidine and succinylsulfathiazole. Sulfapyridine is now considered obsolete and is no longer used in this service, sulfanilamide is rarely employed and only a preliminary report can be given on sulfamerazine, since its use has been recent.

This particular study was undertaken to determine the relative incidence of untoward reactions to the various drugs and the relation of the mild and readily recognizable symptoms to severely toxic or lethal reactions. Difficulties were encountered in this evaluation because many patients admitted to this service are critically ill as the result of acute infection or are in a moribund state of chronic disease, and thus the division of symptoms due to drug and those due to disease is difficult. Also the drug is usually discontinued at the first sign suggestive of sulfonamide toxicity. Consequently the course from early and mild to late and severe symptoms can rarely be followed.

Table 1 shows the relative incidence of toxic reactions and of deaths due to and contributed to by sulfonamides. Persons treated at home and sent to the hospital because of toxic symptoms are excluded, since this would yield an erroneous incidence of toxicity. Untoward symptoms caused by sulfadiazine are significantly less than those due to sulfathiazole and sulfapyrazine.

The symptomatology deserves some description and comment. Although the incidence may vary between one sulfonamide and another, the clinical picture is much the same. Table 2 demonstrates the incidence of the various symptoms and syndromes. It includes patients referred because of sulfonamide intoxication.

TABLE 1.—*Incidence of Toxic Reactions to Sulfonamides in the Medical Wards of the Cincinnati General Hospital, January 1940 to April 1944*

	Patients Treated	Patients Who Developed Toxic Reactions *	Per Cent	Deaths Due to Drug Intoxication *	Deaths in Which Drugs Contributed
Sulfathiazole	1,261	87	6.9	2	4
Sulfadiazine	503	16	3.2	2	0
Sulfapyrazine	132	11	8.3	0	1
Succinylsulfathiazole	18	1	...	0	0
Sulfaguanidine	22	1	...	0	0
Total	1,936	116	6		

* Not counting reactions or deaths that came after home treatment with sulfonamides.

Fever occurs most frequently between the fifth and tenth days of therapy. It is usually above 102 F. and, when chills occur, rises as high as 106 F. The fever may be of a plateau type or may mimic a septic source with daily elevations. In a small number of cases there is a relative bradycardia. The white blood cell count may be as high as 20,000 or may be within normal limits. Unfortunately there is no absolute method, short of discontinuing the sulfonamide, of differentiating such fever from that produced by the infection for which the drug is given. Frequently, however, there are clinical signs of resolution of the infection, or one is aided by the appearance of skin manifestations.

Skin lesions usually appear between the second and tenth days. Sulfathiazole usually produces a tender erythema nodosum, most frequently found on the extensor surfaces of the extremities and on the face. Sulfathiazole may also produce a morbilliform erythematous rash, either localized or widespread. This is similar to the lesions produced by sulfadiazine in 3 cases. The skin lesions may become pustular with continued administration of the drug.

Conjunctivitis, frequently associated with erythema nodosum, occurred only in patients treated with sulfathiazole in our series. It occurred between the fifth and fourteenth days and was bilateral in all but 1 case. The erythema and moderate edema of the bulbar conjunctiva may be accompanied by burning of the eyes and photophobia.

Nausea and vomiting, distressing symptoms that contributed to the discarding of sulfapyridine, occur infrequently with sulfathiazole and rarely with sulfadiazine. It usually appears after the first dose of the drug, in contrast to similar symptoms which may appear later as a result of uremia due to sulfonamide nephrosis or tubular obstruction. It is usually possible to change immediately to another sulfonamide with prompt relief of the emeses.

Polyneuritis, which is usually asymmetrical, has a remarkably high incidence. This may be due to the nutritional state of the patients of the Cincinnati General

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Hospital.[1] Its onset with pains, burning, numbness or tingling has occurred as early as the seventh day of treatment and perhaps as late as six months after a course of sulfonamide.

Delirium is difficult to attribute to sulfonamides, since it occurs so frequently in febrile disorders. As a rule it occurs in association with other toxic manifestations of the drugs, particularly renal complications.

Polyarthritis and arthralgia appeared in a small number of our cases between the second and twelfth days.

Alterations in the blood and bone marrow were noted eleven times in the case of sulfathiazole, once with sulfapyrazine and not at all with sulfadiazine. Others have reported similar reactions with sulfadiazine, however, and we have seen it several times in patients not included in this series. These reactions may occur at any time in the course of therapy. Leukopenia gives no clinical sign. Thrombocytopenia is, of course, usually associated with hemorrhagic phenomena, hemolytic anemia with jaundice, and agranulocytosis with dirty ulcerations of the mouth and pharynx.

injury of the secreting portion of the kidney. In this paper we refer to the former as "calculi" or crystalline obstruction and to the latter as sulfonamide nephrosis. The former has been the most common in this series but has not caused death. All the fatal cases here described were due mainly to nephrosis.

Crystalline obstruction or "calculi" may be asymptomatic, but generally hematuria and sometimes renal colic appear from the second to the eighth day. These signs may be followed by drug retention, oliguria, albuminuria, anuria and uremia. In our group of 30 patients that developed this picture, the smallest dose was just under 3 Gm. of sulfathiazole. We believe a urine p_H of 7 or above and a high urine urea content aid tremendously in elimination of the crystals.

Sulfonamide nephrosis, characterized by drug retention, and a rising blood urea nitrogen may or may not be accompanied by oliguria and anuria and by albuminuria. It has occurred in patients receiving sodium bicarbonate. It may occur in conjunction with a systemic picture of encephalopathy, myocarditis, hepatitis, anemia, leuko-

TABLE 2.—*Symptoms in Relation to Drug and Dosage in the Medical Wards of the Cincinnati General Hospital, January 1940 to April 1944*

	Sulfathiazole				Sulfadiazine				Sulfapyrazine				Succinyl-sulfathiazole			Sulfaguanidine		
			Dose, Gm.				Dose, Gm.				Dose, Gm.							
	Number of Cases	Days of Appearance	Range	Average	Number of Cases	Days of Appearance	Range	Average	Number of Cases	Days of Appearance	Range	Average	Number of Cases	Days of Appearance	Dose, Gm. (Range)	Number of Cases	Days of Appearance	Dose, Gm. (Range)
Fever	43	5-10	16-99	47	2	3-34	42-190	..	2	1-6	13-44	..	1	7	91			
Skin lesions	39	2-10	5-264	45	3	8-34	55-190	..	..	..	.....	..	..	..	..	1	8	23
Calculi	18	2- 7	3-68	27	6	2- 8	8-51	29	6	2-8	14-99	41						
Nephrosis	5	1- 5	6-19	10	3	2- 4	12-58	..	1	5	48	..	..	..	..	1	5	23
Delirium	3	2- 4	26-70	39	1	1	22											
Nausea and vomiting	13	1	8-58	26	..	....	.....	..	1	6	44							
Conjunctivitis	10	5-18	21-103	63														
Hemolytic anemia	4	5-14	40-56	51														
Leukopenia	5	4-10	19-56	32	..	....	.....	..	1	3	17							
Agranulocytosis	2	21	56 *															
Arthritis	1	4	16	..	1	5	24											
Arthralgia	3	2-12	8-99	46														
Neuritis	6†	7 days to 6 mo.	50-197	76	3‡	9-36	27-100	65										
Hepatitis	1																	
Rash with edema	1	13	48															

* Total dose of sulfadiazine, succinylsulfathiazole and sulfathiazole.
† Two patients received sulfadiazine and sulfathiazole; 1 received sulfanilamide, sulfapyrazine and sulfathiazole.
‡ One patient received sulfapyrazine and sulfathiazole.

None of the toxic symptoms are of particularly deadly portent. Most of them disappear within one to two days after discontinuance of the sulfonamide, except that neuritis may not. Leukopenia may disappear even while treatment with the sulfonamide continues. When the onset of peripheral neuritis occurs during treatment, the necessity of treatment must be weighed against the possibility of a persistent neuritis after recovery. Thiamine has not cured or prevented this form of neuritis. Some of our patients developed neuritis while receiving brewers' yeast, thiamine and liver extract. In others, vigorous treatment with vitamins and diet may have prevented neuritis from becoming worse.

Hepatitis, myocarditis and disorders of other systems undoubtedly occur, but as yet our clinical methods of evaluation are too limited to make it possible to be certain in their recognition.

The most troublesome toxic symptoms center about the kidney and the urinary tract. These have been the most dangerous to the patient and most difficult to diagnose in early stages. They appear in two separate forms but may overlap. The one is mechanical obstruction of the renal pelvis or ureter by crystals; the other is

1. Blankenhorn, M. A.: Multiple Peripheral Neuritis Occurring with Sulfonamide Therapy, Ann. Int. Med. **20**: 423 (March) 1944.

cytosis and fever and is readily confused with Weil's disease when the history of sulfonamide ingestion is lacking. It appeared in 10 of the cases collected, and the smallest dose of drug (sulfathiazole) was 6 Gm. It was noted regularly between the first and fifth days that the first manifestation was a rising blood urea nitrogen level.

The treatment of renal complications must suit the individual case. Because of the frequency with which renal complications occur, daily fluid intake and urinary output, and frequent examination of the urine for erythrocytes and blood for drug level and nonprotein nitrogen should be a routine. For hematuria the urine should be alkalized promptly by administration of sodium bicarbonate, and fluids should be administered to bring the urinary output to at least 1,200 cc. per day. If oliguria or retention of drug or nonprotein nitrogen develops, fluid intake should be increased, but if improvement does not result the drug should be discontinued. Ureteral catheterization is indicated if anuria is preceded by hematuria and renal colic. Only 1 of our patients has benefited by this procedure.

The value of routine alkali treatment concomitant with the sulfonamides is still open to question. Although it is true that sulfonamides are more soluble in alkaline

solutions and consequently might have less opportunity of depositing in the genitourinary tract, the increased rate of excretion tends to reduce the blood level of the sulfonamide to below effective range. Of the 30 patients with urinary complications due to sulfonamides, 11 had received alkali by mouth during sulfonamide administration. Four of these so treated were among the 11 who died. Five of the patients who died were given alkali by mouth or parenterally after the appearance of renal failure. Nine of the 11 were given parenteral fluids in an attempt to increase the flow of urine. Dehydration at this stage did not play a significant part.

were not considered to be of clinical significance and occurred infrequently. They included soreness of the neck and shoulder muscles, headache, dysphagia, weakness, malaise and pruritus.

Similar symptoms of toxicity apparently occur with sulfamerazine. Of 86 patients thus far given this sulfonamide, 9 have developed such untoward reactions. Three showed leukopenia, 2 fever, 1 delirium, 1 hematuria alone and 2 nephrosis. The majority of these patients suffered from pneumococcic disease.

Of the 1,936 patients included in the general report, the death of 4 (0.2 per cent) could be attributed mainly,

TABLE 3.—*Deaths Due to Renal Complications of Sulfonamide Therapy in the Medical Wards of the Cincinnati General Hospital, January 1940 to April 1944* *

Name	Age	Sulfonamide	Dose, Gm.	Diagnosis	Primary or Secondary Cause of Death	Early Signs and Symptoms	Late Signs and Symptoms	Autopsy
R. C.	75	Thiazole	22	Bronchopneumonia, arteriosclerosis and hypertensive heart disease, bronchial asthma	Primary	Oliguria, hematuria, general arteriosclerosis	Oliguria, hematuria, azotemia (blood urea nitrogen 165)	Sulfathiazole crystals in tubules and pelves of kidneys and in ureters
V. C.	84	Thiazole	33	Bronchopneumonia, general arteriosclerosis, diverticulitis	Primary	General arteriosclerosis, poor hydration, microscopic hematuria, incontinence, oliguria	Increasing azotemia, drug retention, acidosis	"Acute pyelonephritis due to crystals"
M. T.*	42	Thiazole	6	? Pelvic disease	Primary	Maculopapular rash, stupor, fever, anemia, blood urea nitrogen 35	Oliguria, anuria, drug retention, blood urea nitrogen 165, fever, coma	Kidneys: multiple miliary areas of necrosis. Heart: interstitial myocarditis with few miliary areas of necrosis
A. B.*	49	Thiazole	?	Bronchopneumonia	Primary	Nausea and vomiting	Jaundice, oliguria, hematemesis and melena, stupor, anemia, blood urea nitrogen 182-278	None
G. B.	43	Thiazole	16	Lobar pneumonia type I, bacteremia, miliary pulmonary abscesses	Secondary	Azotemia, drug retention	.....	Active chronic interstitial nephritis; much swelling of tubular epithelium
H. M.	44	Thiazole	34.5	Chronic pyelonephritis, hypertensive cardiovascular disease with encephalopathy	Secondary	Chronic pyelonephritis with urine albumin +++, red blood cells, white blood cells and casts + blood urea nitrogen 38	Blood urea nitrogen 171, drug retention, coma	None
B. H.	76	Thiazole	15	Bronchopneumonia, chronic bronchitis, general arteriosclerosis	Secondary	Dehydration, blood urea nitrogen 48; fixed urine specific gravity, anuria, incontinence	Hyperventilation, carbon dioxide 28	None
G. J.	46	Thiazole	15	Bronchopneumonia, hemolytic streptococcus, empyema, hypertensive cardiovascular disease	Secondary	Severe hypertensive cardiovascular disease. Urine: white blood cells, casts, red blood cells prior to drug, blood urea nitrogen 42, drug blood level 27.5 mg. %	Blood urea nitrogen 149, drug retention, melena (uremic ?), anemia	None
E. R.	86	Diazine	58	Bronchopneumonia, pneumonia type III, arteriosclerotic heart disease	Primary	High level 17 mg. %, general arteriosclerosis	Progressive azotemia, confusion, stupor, coma	Acute bronchitis, bronchopneumonia, cardiac dilatation and hypertrophy; toxic myocarditis; arteriosclerosis; severe toxic nephrosis
H. S.	69	Diazine	51	Lobar pneumonia type I, bronchial asthma, chronic bronchitis	Primary	Arteriosclerosis, microscopic hematuria	Gross hematuria, oliguria, blood urea nitrogen 70	None
R. F.	41	Pyrazine	99	Staphylococcic septicemia	Secondary	Drug level 20 mg. %, oliguria, blood urea nitrogen 59 %	Rising azotemia, anuria, coma	Sulfapyrazine crystals in renal calices, pelves, cortices and medullas and ureters

* Including patients treated at home.

A patient who has toxic symptoms from a specific sulfonamide need not necessarily display signs of toxicity with another. In this series we have been able to find 6 instances in which initial treatment with sulfathiazole resulted in rash, fever, nausea and vomiting or hematuria. All 6 were changed directly to sulfadiazine. In 4 the untoward reactions, including hematuria, subsided immediately. In 2 (fever, rash) the toxic symptoms recurred.

In 2 instances in which sulfadiazine produced azotemia, sulfathiazole was substituted after omission for a few days. The azotemia did not recur. In 1 case, however, after 90 Gm. of sulfathiazole, fever, cutaneous lesions and conjunctivitis appeared.

Numerous minor subjective complaints appeared which could be attributed to the sulfonamides. These perhaps solely, to the action of the sulfonamides. In 5 more instances death was probably hastened by the administration of sulfonamides. To this group are added 2 cases of sulfathiazole intoxication with resultant death in which the drug was given in the home by a private physician. All these patients died with renal complications due to sulfonamides. Six necropsies were performed in this group of 11 deaths.

Table 3 shows the pertinent clinical data including autopsy. In the 6 cases thus examined, obstruction of the pelvis or ureter did not occur. Crystals were recorded as the evidence of sulfonamide intoxication, but crystals or calculi did not obstruct. None of the patients examined post mortem were anuric.

Five of the cases might be classed as nephrosis. In only 2 of these was there an early manifestation of

sensitivity; i. e., in 1 a typical rash developed and in another nausea and vomiting were noted from the first dose.

There were certain signs and conditions in these individuals which warned against indiscriminate use of sulfonamides. Five showed advanced arteriosclerosis and 2 impaired renal function. The earliest manifestations of unfavorable action of the drug were varied and seldom subjective—usually microscopic hematuria, oliguria, incontinence and drug retention. None had renal colic. The signs of uremia later developed.

Although the blood urea nitrogen is one of the most useful of indexes in this problem, its magnitude has apparently little relation to the survival or recovery of the azotemic patient when the drug is discontinued. In one individual who recovered, the blood urea nitrogen rose to 135 mg. per hundred cubic centimeters. In another it was 70 mg. per hundred cubic centimeters on the day of death. Seventeen of those with genitourinary complications who recovered had blood urea nitrogen levels over 50 mg. per hundred cubic centimeters. It has been routine in this medical service to measure the urea nitrogen on all patients before and during treatment with sulfonamides. An initial level as high as 70 or 80 mg. per hundred cubic centimeters does not defer cautious treatment of acute infectious disease. Should the level of nitrogenous products rise constantly however during sulfonamide therapy, it is wise to discontinue the drug regardless of the drug blood level.

It is apparent, then, that with advanced age and renal disease sulfonamides should be prescribed cautiously and the treatment followed carefully. With the onset of persistent hematuria, decreased urine output, signs of azotemia and unusually high levels of sulfonamide in the blood or of any one of these manifestations, treatment should certainly be discontinued.

It is obvious that the early signs of severe reactions are so occult as to be revealed usually only by laboratory studies. There is nothing, unfortunately, that bedside appraisal of the patient will yield in the early diagnosis of the fatal sulfonamide reaction.

SUMMARY

Among 1,936 patients toxic reactions were recorded among 116, an incidence of 6 per cent. These reactions were usually of such severity as to compel the arrest of treatment. Occasionally treatment could be resumed by changing to another drug. This could be done oftenest by changing from sulfathiazole to sulfadiazine.

Death was ascribed to toxic effects mainly in 4 instances (0.2 per cent) and death in 5 was certainly hastened by drug intoxication. All fatal toxic reactions were mainly renal and resulted in uremia.

In no instance was blockage of the pelvis or ureter thought to be the cause. There was no correlation of the milder forms of intoxication to the more severe or lethal.

Therefore there are no premonitory signs of renal intoxication. Mild signs of disease of the kidney pelvis are microscopic hematuria, oliguria, incontinence, pain and elevated blood urea.

If these signs are observed, sulfonamide treatment should be stopped or continued with great care lest nephrosis occur. The use of alkali and water usually corrects mild symptoms. By the time classic symptoms of uremia appeared, no form of treatment was effective. In this series blockage of the renal tubule was considered the cause of death; hence ureteral catheterization was not helpful. In disease of the tubule, symptoms may be absent until the disease is well established and irreversible.

ABSTRACT OF DISCUSSION

Dr. Lawrence D. Thompson, St. Louis: Few reports have covered such a large series of cases and have been so well analyzed as this report by Drs. Vilter and Blankenhorn. The comparative incidence of reactions with the various drugs agrees closely with the majority of reports. The report of Hageman, Harford, Sobin and Ahrens from our clinic revealed little difference in the incidence of reactions following the use of sulfadiazine and sulfamerazine. My own observations, although covering a series only about one third as large, are in close agreement with those reported, with a possible exception in the cases of renal complications; the incidence of these complications has been somewhat smaller. It is accepted that age and preexisting renal damage predispose to renal complications following the use of sulfonamide drugs. Since most of the cases were observed in the St. Louis City Hospital, this series should be comparable to that of Vilter in respect to this factor. The forcing of fluids is also a generally accepted part of sulfonamide therapy. The deliberate limiting of fluid intake in order to secure a high blood level of the drug early in the course of treatment is to be condemned most emphatically; unfortunately, this tendency has appeared repeatedly during the past year. The use of sodium bicarbonate may have contributed to this difference in results. The wisdom of the routine use of sodium bicarbonate is still under debate. The increased solubility of the drugs in alkaline urine is undisputed. The early observations of Hartmann and his co-workers, which indicated the harmful effect on the kidneys of an alkalosis combined with the use of sulfanilamide and sulfapyridine, made such an impression on me that only rarely have I given sodium bicarbonate. Later studies have made it clear that sulfanilamide and the more recent sulfonamides cannot be compared in many respects. Perhaps it was an error to apply this rule with the use of sulfathiazole and sulfadiazine; however, like sulfanilamide, these drugs are reabsorbed to a significant extent by the renal tubules. This reabsorption has been shown to be an active process by the tubular cells. The harmful effect of either acidosis or alkalosis on already impaired tubular cells has been pointed out by many students of renal physiology and pathology. Until more exact information is available, it is logical to assume that two agents, each of which in itself may impair renal tubular function, should not be used together except for some very special purpose and then under most careful observation. The repetition of observations on the toxicity of these drugs, particularly as to the effect on the renal tubules, such as the work of Shannon under the experimental condition of deliberate alkalosis, might throw some light on this debated point.

Dr. S. L. Bernstein, Cleveland: What is Dr. Blankenhorn's opinion of the administration of the sulfonamide drugs on ambulatory patients? I recall giving a man aged 60 a small dose of sulfanilamide for a septic throat, without a culture. He had a total of 20 grains (1.3 Gm.), with alkali, for three days. He had to be urged to go to the hospital because of agranulocytosis. Fortunately, he recovered. Since then I have been chary about prescribing sulfonamides to ambulatory patients. One sees many prescriptions at the drug stores, with doctors prescribing them for ambulatory patients. The druggists are beginning to prescribe them over the counter, and this is becoming a serious question.

Dr. David Lehr, New York: In experiments on the prevention of renal obstruction, the animals received repeated intraperitoneal injections of sodium sulfadiazine in amounts known to produce massive precipitation of sulfadiazine in the renal tubules, provided no therapy was employed. Stomach tube feedings of water alone did not provide adequate protection. Animals of this group succumbing to the sulfadiazine intoxication revealed without exception massive intratubular precipitation

of sulfadiazine accompanied by severe tubular dilatation and degeneration of the kidneys. The striking success of alkalization (sodium bicarbonate) in combination with the "forcing of fluids" was clearly borne out by the high rate of survival (no death) and the almost complete absence of significant pathologic lesions in the alkali treated animals. These measures were of little value once the renal obstruction was fully developed. In such instances the "forcing of fluids" actually produced water poisoning. In the treatment of renal obstruction, standardized experimental conditions were established in the following manner: The renal block was produced by intraperitoneal injection of a single fatal dose of sodium sulfadiazine. If left untreated, the animals invariably developed pronounced renal obstruction from intratubular precipitate of sulfadiazine, and 80 to 90 per cent succumbed to this complication after two to three days. Treatment consisted in stomach tube feedings of fixed amounts of water or salt solutions (containing either sodium bicarbonate, ammonium chloride, a mixture of these two or sodium chloride). The most striking result was achieved with solutions of sodium chloride and of the mixture of sodium bicarbonate and ammonium chloride. They made possible the complete recovery of all rats from an otherwise fatal sulfadiazine intoxication, whereas no benefits were derived from the "forcing" of water alone. The water-sodium bicarbonate combination even shortened the time of survival (alkalosis), and ammonium chloride, in addition to a further reduction of the life span, also increased the mortality to 100 per cent (acidosis). Apparently water alone is reabsorbed rapidly under the conditions of a block in the collecting tubules, whereas in the presence of salts of high osmotic value some of the water might be forced to remain in the tubules, dilate them and push the tubular plugs down and out of the kidney. The life saving effect of salt diuresis in renal obstruction from sulfadiazine has been learned in experiments with more than 200 animals.

DR. M. A. BLANKENHORN, Cincinnati: Dr. Thompson and I come to the same consideration of the problem of the general practitioner who gives sulfonamides; namely, damage to the kidney. The matter of making alkalis mandatory with sulfonamide medication is a weighty one, and being responsible for rather a large service with a great variety of patients and a great variety of house officers, I am unwilling to make it mandatory in the service for the reasons of which Dr. Thompson mentioned a few. Perhaps we might have improved our service had we been able to give alkalis intelligently. Merely to exhibit alkalis to the patient is far from meeting the indications of alkalizing urine. Alkalis may be given in too great an amount, and they may be given in an insufficient amount. The object is to alkalize the urine. We used nitrazine paper to test the urine, when freshly voided, as our criterion of alkalization. That is a simple device which any general practitioner can put into the hands of his nurse. Litmus paper is not reliable. I may have been misleading in my discussion of the treatment and the prophylaxis of renal complications in mentioning water. Dr. Lehr, when I said "water" I meant water as a vehicle for glucose, saline, alkali in the form of bicarbonate and lactate. To answer Dr. Bernstein on the use of sulfonamides for ambulatory patients, if I should draw on my own experience I would be absolutely against it. I have seen individuals carried into the hospital in a desperate condition, and I have not counted the deaths that I have seen in other hospitals where ambulatory patients had been treated or received. There are several in my experience, and my advice would be not to give it to ambulatory patients. I am not unfamiliar with Dr. Lehr's work and with the work of others who have concentrated on the function of the tubule and its reaction to this drug, because that is where the work must be done, and it is from such experimentation that the answer may come. The use of alkalis in moderate dose, in advance of treatment or with treatment, will not always prevent fatal damage to the kidney. I speak particularly of that lesion of the kidney which involves the parietal structure of the kidney, as well as the tubule. That is a cellular infiltrate resembling granuloma. Just why that lesion occurs, I do not know. Two of the patients not counted in this series that I have seen had that disorder of the kidney from relatively small doses. That was the unfortunate individual who is sensitive to the dose and has perhaps an allergic reaction.

THE SIGNIFICANCE OF MUSCLE SPASM

IN THE ACUTE STAGE OF INFANTILE PARALYSIS BASED ON ACTION CURRENT RECORDS

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The total time interval required for essential agreement on some phases of infantile paralysis includes the names of Heine,[1] Medin,[2] Wickman,[3] Lovett[4] and many others. During this period and since that time a steady flow of literature has provided evidence of the great efforts which have been made in the study of all aspects of a disease which annually disables great numbers of children and adults.

Out of all this there came the confirmation of a correlation between the pathologic changes and the clinical characteristics of infantile paralysis. Thus it became established that the disabilities provoked by this disease were directly proportional to the degree and extent of permanent damage to the lower motor neurons on which normal muscle function was dependent.

Spasm in the muscles of the neck and back, the spine sign, was a noted characteristic of early onset. Hyperesthesia was less frequent but carefully distinguished from muscle soreness, tenderness and pain. The latter usually prevailed but was most variable as related to degree and duration.

In 1916 Lovett[5] and, more recently, Ober[6] and others have recorded the observation that moist heat relieves muscle pain and soreness. The prescription of rest for the affected extremity was then logically based on principles which are today recognized as sound practice in all phases of clinical medicine and surgery.

When considered as a unit, each of three parts, (1) the pathologic characteristics, (2) the clinical manifestations and (3) the treatment, were related so naturally in the form of a premise that they have held together with ease for more than three decades.

But none of us would hesitate to divorce ourselves from this or any other premise when presented with the evidence that it was wrong. However, any logical premise which has slowly developed from the work of many men in various countries should not be readily discarded on the basis of a different opinion which depends solely on clinical observations relevant to some particular manifestation of a disease.

This brings us to Sister Kenny's concept of infantile paralysis. It is based on her personal observation of

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1. Heine, J.: Beobachtungen über Lähmungezustande der unteren Extremitäten und deren Behandlung, Stuttgart, F. H. Kohler, 1840.
2. Medin, O.: Ueber eine Epidemie von spinaler Kinderlähmung, Verhandl. d. internat. med. Cong. (1890) **2**: 37, 1891; Infantile Paralysis with Especial Reference to Its Acute Stage, Nord. med. Ark. **6**: No. 1, 1896; translated, Arch. de méd. d. enf. **1**: 257 and 321, 1898.
3. Wickman, I.: Studien über Poliomyelitis acuta: Zugleich ein Beitrag zur Kenntniss der Myelitis acuta, Berlin, S. Karger, 1905; reviewed, Arch. de méd. d. enf. **9**: 636, 1906.
4. Lovett, R. W., and Richardson, M. W.: Infantile Paralysis, with Especial Reference to Its Occurrence in Massachusetts, 1907-1910, Am. J. Dis. Child. **2**: 369 (Dec.) 1911.
5. Lovett, R. W.: The Treatment of Infantile Paralysis, ed. 1, Philadelphia, P. Blakiston's Son & Co., 1916; ed. 2, 1917
6. Ober, F. R.: Pain and Tenderness During Acute State of Poliomyelitis, J. A. M. A. **120**: 514 (Oct. 17) 1942.

patients during and after the acute stage of the disease. In Pohl's [7] most recent book on the subject it is stated that:

> Infantile paralysis is neither a simple disease nor one completely understood. The destruction of anterior horn cells of the spinal cord is certainly not the principal nor the most important characteristic and does not explain the presenting symptoms of the disorder. From the discussion presented, infantile paralysis affects both muscles and nerve tissue and is a disease capable of widespread disorganization of the neuromuscular system. The condition of muscle spasm is the symptom common to all cases. Untreated spasm destroys muscle tissue and is the cause of contractures, stiffness and deformities. In addition, the pathophysiological symptoms of mental alienation of muscle and incoordination of muscle action implicate the more highly organized portions of the nervous system. Paralysis is unfortunately a feature of the disease, but paralysis proves after all to be a minor consideration in most cases of infantile paralysis. Muscle spasm, mental alienation and incoordination are far more damaging to bodily mechanics. Acceptance of these true symptoms forms the true basis on which the treatment of the disease can be designed. Only meticulous attention to all of the disturbed structures can reduce the evil after-effects of the disease.
>
> Spasm . . . if untreated will result in permanent muscle damage, stiffness and skeletal deformities.
>
> . . . muscle spasm in the acute stage appears almost to have the properties of an acute inflammatory process capable of causing serious and permanent changes in the muscle substance.
>
> . . . the examination of the patient should not include stretching, squeezing or manipulation of the affected muscles, nor should the patient be requested to make any voluntary efforts at contraction of the muscle.
>
> It is recognized that certain muscles, noticeably the opponents of the muscle in spasm, have become nonfunctioning. This is of no immediate concern, since these nonfunctioning muscles *usually* are simply alienated. Such muscles, however, cannot be restored except by first treating the condition of spasm in the opponent. Attempts to determine the presence or absence of contractile power in muscle are therefore not only impossible and of no value, but they have the serious effect of increasing the spasm in the affected muscles. Under no circumstances should the acutely ill patient be encouraged to contract any of his muscles for the purpose of recording the so-called muscle test.
>
> Inspection or observation alone usually suffices for the purpose of analysis of the muscle condition.
>
> Critical examination of infantile paralysis in the acute stage will present abundant evidence to show that orthodoxy has erred both in the recognition as well as in the interpretation of the physical findings of the disease.
>
> Miss Kenny's real contribution is not a new treatment for the disease of infantile paralysis as it has been conceived in the past but a conception of the disease itself so radically opposed to the old as to almost warrant considering the entity as a new disease. The basic principles . . . [are] . . . built upon observations of the behavior of the musculature. . . .
>
> In short, Miss Kenny's discovery is that infantile paralysis is a disease in which disturbance of physiological function of the nervous system is of more importance than actual architectural change. Many of the observable clinical phenomena are the result of functional disorganization of the motor centers and of the nerve pathways to the muscles. The disease affects muscle as well as nerve tissue. Muscle spasm is the primary lesion in the disease rather than paralysis. Miss Kenny has designed a treatment for these conditions. Needless to say, the treatment could have nothing in common with the previous methods, designed for a disease of opposite conception.

7. Pohl, J. F., and Kenny, E.: The Kenny Concept of Infantile Paralysis and Its Treatment, Minneapolis, Bruce Publishing Company, 1943, pp. 37-38, 59-60 and 61-62.

Any concept such as this one should not be accepted or rejected on the basis of clinical observation alone. An objective analysis of the new versus the old concept revealed a common agreement on one point; i. e., neuromuscular dysfunction was the cause of disabilities and therefore continued to be the reason for the great efforts made to bring infantile paralysis under control. This point in common should therefore lead to agreement that a lowering of incidents of disabilities, subsequent to the acute onset of the disease, is dependent on the discovery of more effective methods of preventing the impairment of muscle function. From this point it naturally follows that a continuation of past efforts toward this objective might be favored by additional information regarding the behavior of the neuromuscular mechanism in the acute stage of infantile paralysis.

It therefore became our purpose to investigate the characteristics in the behavior of the neuromuscular mechanism, primarily as related to the acute stage of infantile paralysis, for comparison with the recorded characteristics of normal individuals and the records of patients with other established neuromuscular disabilities. In so doing it was indicated that we should pay particular attention to any and all evidence through which the significance of muscle spasm might be evaluated.

Here we venture to state that a similar point of view may have prompted the electromyographic studies made by Watkins, Brazier and Schwab.[8] It was gratifying to note the agreement between their recorded evidence and that which we reported in 1942.[9] This fact is far more important than that we offer a slightly different explanation for the recorded abnormal functions of the lower reflex arc.

With the introduction of muscle spasm as the dominant influence contributing to disability, the authors previously quoted also accepted the possibility of paralysis on the basis of established evidence of partial damage to or complete destruction of the lower motor neuron innervation, in part or in toto, to one or more muscles. The absence of conclusive evidence in support of the statements which have been quoted regarding muscle spasm cannot be regarded as evidence that spasm might not play a significant role in producing disabilities. However, the clinical and myographic records of muscle spasm in the acute stage of infantile paralysis should not be interpreted as evidence which confirms the "new concept" as quoted.

But this "new concept" has already been found to be at variance with the distribution of spasm as recorded by action currents through the oscillograph. Our original report and that of Watkins, Brazier and Schwab emphasized that muscle spasm in the acute stage of infantile paralysis was not limited to the "antagonists of nonfunctioning muscles." On the contrary, both of these investigations gave evidence which emphasized the presence of spasm in the "nonfunctioning" or weakened muscle and in muscles which showed no clinical or other evidence of weakness, as indicated by successive records from respective patients.

In attempting to clarify this situation we have found that available methods for evaluating the role of muscle spasm are very limited. But it is evident that both mus-

8. Watkins, A. L.; Brazier, M. A. B., and Schwab, R. S.: Concepts of Muscle Dysfunction in Poliomyelitis, Based on Electromyographic Studies, J. A. M. A. **123**: 188 (Sept. 25) 1943.

9. Schwartz, R. P., and Bouman, H. D.: Muscle Spasm in the Acute Stage of Infantile Paralysis, as Indicated by Recorded Action Current Potentials, J. A. M. A. **119**: 923 (July 18) 1942.

cle weakness and muscle spasm are respective states of abnormal function which are expressed through the lower motor neuron. To differentiate between these two states of abnormal muscle function it was found that action current records provided the most useful evidence.

Four action current amplifiers were constructed for use with a multiple recording oscillograph, for making records of the reaction on one or a maximum of four muscles simultaneously, to stretch reflex or voluntary contraction.

A total of 50 individuals have been studied: normal subjects 9, spastic paralysis patients 6, infantile paralysis patients 23, miscellaneous patients 12. The total number of records has been from Nov. 22, 1941 to July 1, 1943 3,622 and from July 1, 1942 to July 1, 1943 2,879.

The past year's work has added confirmation to the summary of recorded evidence reported in 1942 and provides a more lucid interpretation of this evidence than has heretofore been possible. Naturally this approach directs primary attention to prevailing abnormalities in the function of the neuromuscular mechanism of the lower reflex arc during the acute stage of infantile paralysis.

However, a satisfactory understanding of the recorded reactions which are to be enumerated cannot be provided by the simple concept of upper and lower motor neurons without designation of the mechanisms which may be altered by the direct or indirect effect of the virus of infantile paralysis to produce the respective abnormal functions.

Interpretation in this instance should be based on the present available information concerning the intrinsic structures and function of the normal lower reflex arc. This should include information concerning the normal structural and functional relationships which the lower motor neuron bears to other nerve cells at its own and at other levels; i. e., its relation to all neuronal pathways which make essential contributions to every physical effort that requires muscular coordination.

As this information is still in a formative state, our interpretation must be based on the knowledge which is available at the present time.

As part of the spinal reflex arc and as the effector cell of "the final common path," the lower motor neuron plays an obviously essential role in all reflex and voluntary contractions of skeletal muscle. The fact that the lower motor neuron can be excited to discharge by impulses passing over the dorsal spinal nerve roots is axiomatic. That these dorsal root impulses can excite the cell directly or through the medium of interneurons seems established by the investigations of Renshaw[10] and of Lloyd.[11] In addition, the lower motor neuron is bombarded by volleys of impulses passing over pyramidal and extrapyramidal pathways, these impulses reaching the motor neuron probably through the medium of interneurons.

It is important for the lower motor neurons to respond to impulses which reach them, but it is just as important that these same neurons at times should be rendered inactive. An example of this phenomenon is the well known fact that under certain circumstances sensory impulses passing into the spinal cord are prevented from exciting the lower motor neurons to discharge, and these sensory impulses may even block or nullify the effect of other impulses impinging on the motor neuron from other levels of the nervous system. This phenomenon of inhibition leads to the relaxation of antagonists during the performance of muscular movements and thus facilitates their proper execution. At present we have no generally accepted explanation of the mechanism of the inhibitory process. It appears that the functional reaction of the lower motor neuron as related to transmission of impulses by way of the axon to striated muscle fibers is determined by some mechanism at or related to internuncial cells or to the many synapses associated with the dendrites and cell body of the lower motor neuron.

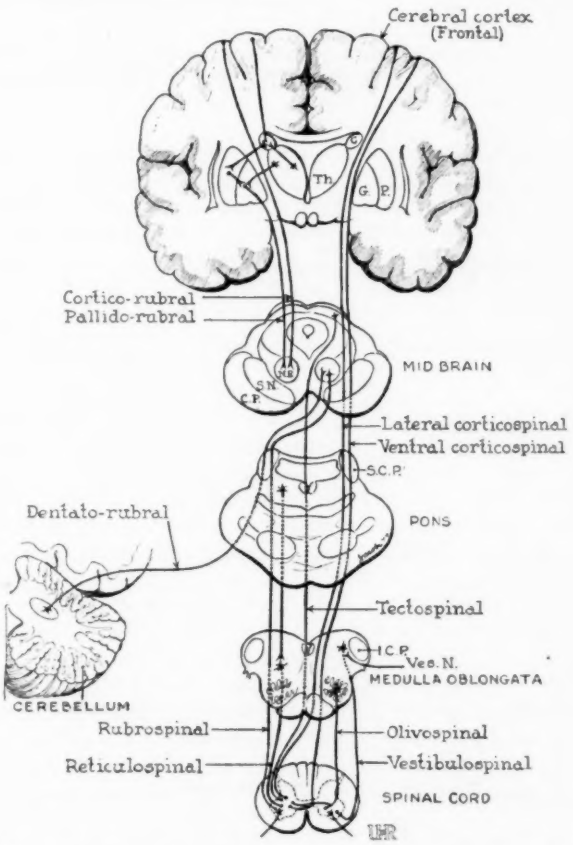


Fig. 1.—Diagram showing some of the descending pathways which influence the spinal motor neuron: *C*, caudate nucleus; *C. P.*, cerebral peduncle; *G.*, globus pallidus; *I. C. P.*, inferior cerebellar peduncle; *N. R.*, red nucleus; *P*, putamen; *S. C. P.*, superior cerebellar peduncle; *S. N.*, substantia nigra; *Th.*, thalamus; *Ves. N.*, vestibular nerve.

In figure 1 some of the pathways through which the lower motor neuron receives a multiplicity of inhibitory and excitory impulses are diagrammatically indicated.[12] The large number of synaptic connections which the lower motor neuron makes with internuncial cells and the axons of dorsal root ganglion cells is in sharp contrast to the single axon over branches of which the former sends impulses to more than one hundred muscle fibers at the rate of five to ten per second for the maintenance of normal tone and at a greater frequency for increased muscular contraction.

When considered as a unit, the cell body of the motor neuron, while making numerous synaptic connections, is regarded as essentially free from structural connec-

10. Renshaw, B.: Activity in Simplest Spinal Reflex Pathways, J. Neurophysiol. **3**: 373, 1940.

11. Lloyd, D. P. C.: Reflex Action in Relation to Pattern and Peripheral Source of Efferent Stimulation, J. Neurophysiol. **6**: 111, 1943; Neuron Patterns Controlling Transmission of Ipsilateral Hind Limb Reflexes in Cat, ibid. **6**: 293, 1943; Conduction and Synaptic Transmission of Reflex Response to Stretch in Spinal Cats, ibid. **6**: 317, 1943.

12. Although we use the term inhibitory impulses, there is no evidence to indicate that impulses causing inhibition differ in any way from those causing excitation.

tions with other neurons which combine to form the neural mechanism for normal muscular control. It is at this level, proximal to the dendrites and the motor cell body, that internuncial cells are present and to them has been largely assigned the function of transmission or rejection of impulses through to activate the motor

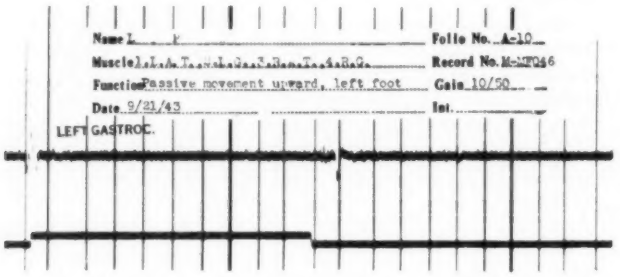


Fig. 2.—Reaction to stretch (stretch reflex) of the left gastrocnemius muscle of a normal person. Upper line, action currents of gastrocnemius muscle; lower line, signal indicating duration of stretch line in all records: 0.1 second and 1 second (heavy line).

cell from which impulses are sent via its axon to the muscle. In addition, the physiologic state of the motor neuron itself is also a determinant factor as to whether or not it is excited to discharge by impulses impinging on it.

In a much less literal sense we may regard the multiple branching axon terminals of the lower motor neuron as somewhat separated from each of the more than one hundred muscle fibers thus innervated. Reference is here made to the non-neural character of the "sole plate," i. e. the group of cells which forms the structural connection between the axon terminals of the lower motor neuron and the striated muscle fibers.

The addition of the sensory relationship to the lower motor neuron-muscle complex is required to complete the elements essential for a simple spinal reflex arc. The "knee jerk" is frequently cited as a typical spinal reflex. Likewise it is an example of the stretch reflex and has proved to be both an important and a fundamental means of eliciting information. By stretching the muscle with a blow on the patellar tendon from a percussion hammer, afferent impulses normally pass from the muscle to sensory ganglion cells of the second to the fourth lumbar and thence to the lower motor neurons, the axons of which transmit the impulses to the quadri-

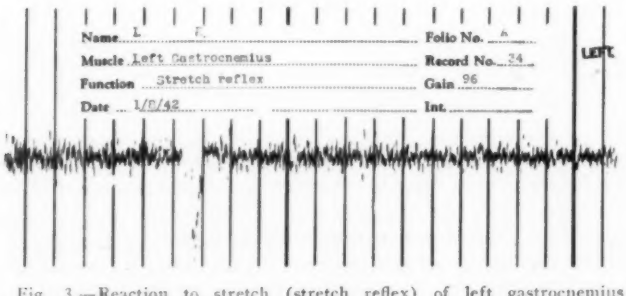


Fig. 3.—Reaction to stretch (stretch reflex) of left gastrocnemius muscle of patient with infantile paralysis.

ceps muscle, which contracts to produce extension at the knee joint. The investigations of Renshaw [10] and of Lloyd [11] show that within a single spinal segment the large nerve fibers conducting afferent impulses from muscle receptors over the dorsal spinal roots synapse directly with the lower motor neuron without the mediation of internuncial cells, thus creating a two neuron arc reflex pathway. In contrast, reflex discharges over the ventral roots, as a result of impulses from cutaneous receptors, appear to involve a multineuron reflex arc including internuncial cells interposed between the axon of the sensory cell and the lower motor neuron. It is of course not possible at the present time to be certain that all of the fibers carrying impulses from the muscle receptors synapse directly with the lower motor neurons or that all of the fibers carrying impulses from cutaneous receptors form connection with the lower motor neuron by means of interneurons, but evidence indicates that such is probably the case in animals under experimental conditions.

By this brief summary of influences under which the lower motor neuron exercises its normal function, our appreciation for the systemic manifestations of infantile paralysis is in no way lessened. Moreover, we are fully aware that repeated observations of the past thirty years have continuously emphasized the effects of the virus of infantile paralysis at nearly all levels of the central nervous system. But, without the associated impairment of muscle function this disease would become relatively unimportant.

However, as related to the latter point our attention must continuously be focused on the functional disturbances of the lower reflex arc as they have been found to prevail in relation to muscle spasm with or without muscle weakness, during the acute stage of

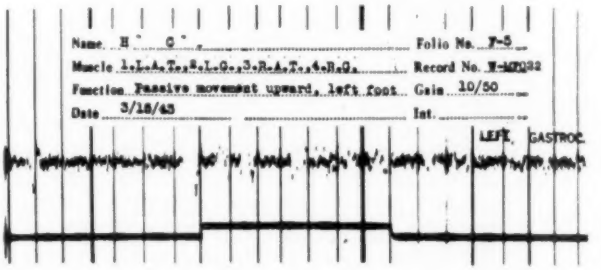


Fig. 4.—Reaction to stretch (stretch reflex) of left gastrocnemius muscle of a patient with spastic paralysis: upper line, action currents of left gastrocnemius muscle; lower line, signal indicating duration of stretch.

infantile paralysis. The stretch reflex of a normal lower reflex arc always produces a characteristic action current record as in figure 2. For this reason, departure from this characteristic action current reaction indicates that abnormal conditions prevail somewhere within or related to the lower reflex arc.

In muscles examined during the acute stage of infantile paralysis, the stretch reflex usually produces a record indicating the prolonged contraction of muscle fibers, as related to both time and degree (fig. 3). This abnormal reaction to the stretch reflex is the phenomenon which we have interpreted as muscle spasm in the acute stage of infantile paralysis.

Here it should be emphasized that the magnitude of spasm thus recorded is in no way comparable to that which we clinically observe, as in spastic paralysis and the like (fig. 4), so readily revealed by both clinical examination and the characteristic dysfunction which it produces.

These characteristics of muscle spasm, which we have recorded in almost every instance, have usually been of such low magnitude that there was seldom agreement between various individuals on clinical examination. However, we have on rare occasions seen intermittent contractions in an anterior tibial muscle. The tendon became prominent at the rate of ten to fifteen times per minute, for a period of twenty minutes in one

instance. The boy, aged 6, stopped crying when the spasmodic contractions of the anterior tibial muscle ceased.

But evidence of spasm was never present when a muscle literally failed to give any action current response to the stretch reflex. In all such instances the muscle was considered as completely paralyzed at the time the record was made. This was regarded as an important observation. It provided a starting point from which we begin to answer questions regarding the evidence of spasm when it is expressed in association with weakened muscles or muscles of normal strength.

From this finding we may conclude that the prevailing evidence of spasm is not due to the intrinsic reaction of muscle fibers as it has been described in association with inflammation or the fibrillation which is said to follow section of the motor nerve to a muscle. We are therefore forced to conclude that in this instance the muscle is deprived of all motor impulses without any associated muscle fiber contractions. An oscillographic record of a completely paralyzed muscle showing no evidence of action current reaction to a stretch reflex is illustrated in figure 5.

The characteristic pattern of a weakened muscle's reaction revealed that its response to voluntary contraction stimulus was often less than the spasm which followed stimulation by stretch reflex.

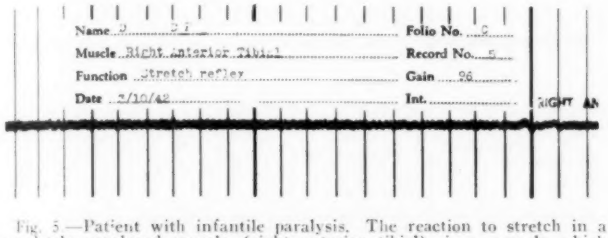


Fig. 5.—Patient with infantile paralysis. The reaction to stretch in a completely paralyzed muscle (right anterior tibial), i. e. muscle which shows no evidence of action currents in maximal voluntary effort.

This has been found to be a common behavior of weakened muscles. There are two plausible interpretations: (1) that more lower motor neurons are stimulated by the stretch reflex than the number which is activated by the voluntary effort to contract the weakened muscle; (2) that, although an equal number of lower motor neurons are stimulated in each instance, a greater number of impulses are induced by the stretch reflex than result from voluntary effort.

This evidence further indicates that voluntary impulses from proximal centers may be more effectively blocked than the sensory impulses which are stimulated by the stretch reflex. From this, therefore, one might conclude that the damage of lower motor neuron cells is not as great as the initial loss in voluntary function would indicate. From this it would follow that impairment of muscle function in the acute stage of infantile paralysis may be due to any one or any combination of the following causes: (1) injury or death of the lower motor neuron cell body; (2) partial or complete block of voluntary impulses from higher centers without damage to the lower motor neuron cell; (3) inhibition of contraction due to the presence of impulses arising within the muscle, i. e. muscle soreness and pain, and that muscle spasm does not initiate the development of muscle weakness as indicated by clinical observation and the following action current records.

The "nonfunctioning" or weakened muscle usually produces a characteristic pattern in response to voluntary and reflex stimulation. The voluntary contraction of the left gastrocnemius muscle, free from clinical evidence of weakness, is illustrated in figure 6 *A*. The voluntary contraction of the weakened right gastrocnemius muscle, same patient, is illustrated in figure 6 *B*. It is apparent that there was much less response in the weakened muscle than in the normal muscle. On

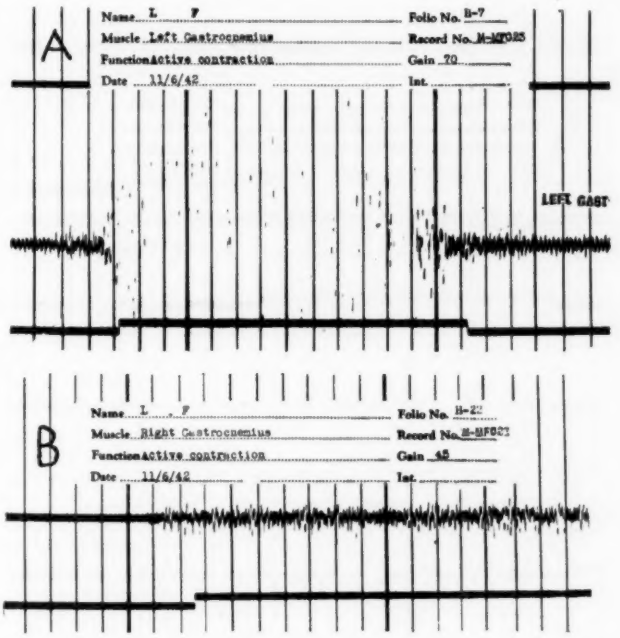


Fig. 6.—Patient with infantile paralysis: *A*, record of maximal voluntary contraction of relatively normal left gastrocnemius muscle; upper line, action currents of left gastrocnemius; lower line, signal indicating duration of movement. *B*, record of maximal voluntary contraction of weakened right gastrocnemius muscle; upper line, action currents of right gastrocnemius; lower line, signal indicating duration of movement.

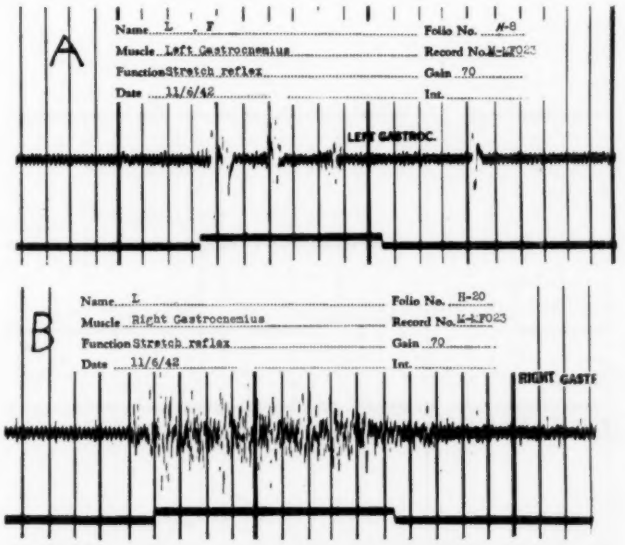


Fig. 7.—*A*, same muscle as figure 6 *A*: record of reaction to passive stretch; upper line, action currents of left gastrocnemius; lower line, signal indicating duration of stretch. *B*, same muscle as figure 6 *B*. Record of reaction to passive stretch (stretch reflex); upper line, action currents of right gastrocnemius; lower line, signal indicating duration of stretch.

stretch reflex of the muscle with normal strength a low magnitude of spasm, as previously defined, was recorded as in figure 7 *A*, while the stretch reflex of the weakened muscle, figure 7 *B*, produced spasm greater in degree than the reaction of the same muscle to voluntary effort as recorded in figure 6 *B*.

In either situation it follows that estimation of the voluntary contraction strength of a weakened muscle does not provide a reliable index of the total capacity of the lower motor neurons which activate the muscle.

As a companion to this reaction there was another which was unanticipated. When the stretch reflex

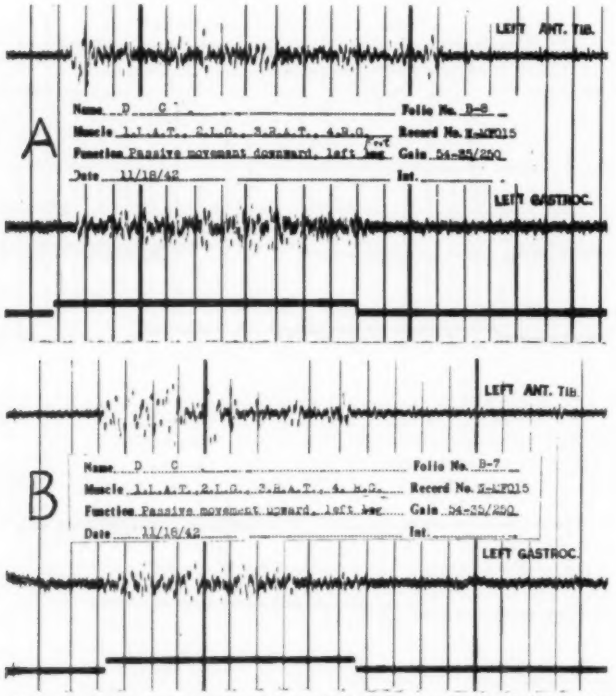


Fig. 8.—Patient with infantile paralysis: *A*, reaction in left anterior tibial and gastrocnemius muscles to stretch of left anterior tibial muscle; upper line, action currents of left anterior tibial muscle; middle line, action currents of left gastrocnemius muscle; lower line, signal indicating duration of stretch. *B*, records from same muscles; record of passive stretching of left gastrocnemius.

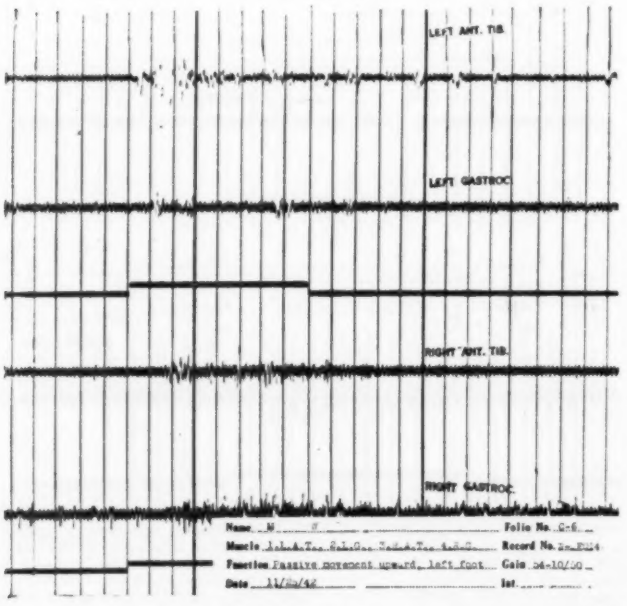


Fig. 9.—Patient with infantile paralysis: Record of action currents of both anterior tibial and gastrocnemius muscles in passive stretch applied to left gastrocnemius; top line, action currents of left anterior muscle; second line, action currents of left gastrocnemius; third and sixth lines, signal indicating duration of stretch; fourth line, action currents of right anterior tibial; fifth line, action currents of right gastrocnemius.

reaction of a weakened left anterior tibial muscle was recorded simultaneously with its antagonist, evidence of spasm was definite in the records of respective muscles (fig. 8 *A*). Likewise when the gastrocnemius was subjected to stretch reflex, there was recorded evidence of spasm in both the weakened muscle and its antagonist as illustrated in figure 9 *A*. This evidence has been interpreted as a reversal of Sherrington's principle of reciprocal innervation. The action current response of a normal left anterior tibial muscle to a stretch reflex applied to its antagonist, the left gastrocnemius, is illustrated in figure 10.

It was observations such as these which emphasized the need for recorded evidence of the reaction of four muscles simultaneously when the stretch reflex was applied to one of the four. Action current records were therefore made as indicated in figure 9. In this instance the stretch reflex was applied to the left gastrocnemius and evidence of spasm was recorded in both the gastrocnemius and the anterior tibial on the left leg and in the corresponding muscles of the right leg. The prevailing evidence of spasm in muscles of the side opposite to the applied stimulus is in sharp contrast with the corresponding reaction of normal muscles as indicated in figure 12. We have also found that the same cross stimulation was provoked by voluntary contraction of the left gastrocnemius, figure 13. A diagrammatic expression indicating how the prevailing dysfunction may provoke this particular behavior on the part of the lower reflex arc is presented in figure 11.

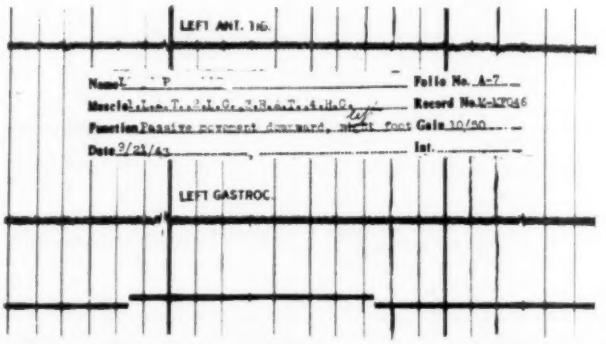


Fig. 10.—Record of same muscles as in figure 8 in a normal person on passive stretch applied to left anterior tibial.

The evidence presented, therefore, indicates that during the acute stage of infantile paralysis the normal function of the lower reflex arc is grossly altered. Such alteration is clinically expressed by partial or complete loss of muscle function. It is also revealed in action current records indicating the presence of spasm in weakened muscles and muscles of normal strength, when respective muscles are stimulated by stretch reflex. It is further emphasized by reversal of the Sherrington reciprocal innervation together with cross stimulation of agonist and antagonist when one of the corresponding muscles on the opposite side is stimulated by stretch reflex or voluntary contraction. But it should be emphasized that this recorded evidence of altered function, (1) spasm, (2) reversal of the Sherrington reciprocal innervation and (3) cross stimulation, all gradually disappeared subsequent to the passing of muscle soreness and pain, which is not always present but when present is always first to disappear. If and when disabilities prevail in the postacute stage, they are expressed in terms of muscle weakness or complete paralysis, usually the former, without clinical or recordable evidence of (1) spasm, (2) reversal of the Sherrington reciprocal innervation or (3) cross stimulation herewith described.

It is during the earlier months of the postacute stage that initially paralyzed muscles may show some return of function and weakened muscles usually regain an appreciable percentage of normal strength. It has been emphasized for fully three decades that such spontaneous improvement is most likely to express itself during the first six months after onset, the rate of improvement thereafter declining during the next six to twelve months.

Such evidence of improvement in strength of a weakened muscle is revealed in action current records of voluntary contraction against resistance of the observer's hand (fig. 14 *A* and *B*). We have found that muscle spasm, stimulated by stretch reflex, diminishes during this period (fig. 15 *A* and *B*). But it does not follow that the disappearance of spasm is necessarily accompanied by full restoration of strength in the weakened muscle. Action current records of weakened muscles, made one to four years after onset, revealed the weakness of voluntary contraction but failed to show evidence of spasm in any of the various manifestations herewith presented as common to the acute stage.

From the interpretation of records let us turn to the clinical record on which the Kenny concept is solely dependent. In 1932 work done by the International Committee on Infantile Paralysis [13] represented a critical analysis of more than 8,000 references. All authorities agreed on the high incidence of muscle spasm in

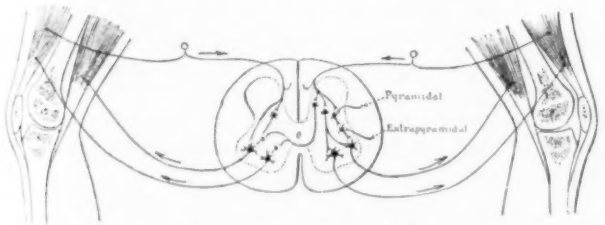


Fig. 11.—Diagram showing some of the neurons involved in a spinal reflex. Only one level of the second to fourth lumbar region which contributes to the knee jerk is shown. Other levels of the spinal cord show similar connections. For explanation see text.

the neck and back as characteristic of the early onset of infantile paralysis. But despite this fact it was also noted that the incidence of muscle function impairment in the neck and back was much less than at any other levels of the body. Wernstedt's [14] figures on 5,948 cases are typical of the percentage distribution of Lovett and other authorities: cranial nerves 13.3 per cent, throat and neck muscles 5.8 per cent, trunk 27.8 per cent, arm 41.3 per cent and leg 78.6 per cent. Lovett's [15] total of 1,529 cases gave the following distribution: one or both legs (with or without one or both arms) 83.3 per cent, one or both arms (with or without one or both legs) 38.7 per cent, abdomen 72.0 per cent, back 13.5 per cent and neck 11.0 per cent.

The common stiffness and less frequent rigidity of the neck and back was invariably accompanied by muscle soreness and pain. The presence of the latter in the extremities was noted to prevail before the onset of muscle weakness or paralysis if and when either became apparent. But the presence of muscle spasm in the extremities was not noted and emphasized as it was in relation to the neck and back.

Moreover, from the inverse relationship of the maximum degree of muscle spasm prevailing in the acute

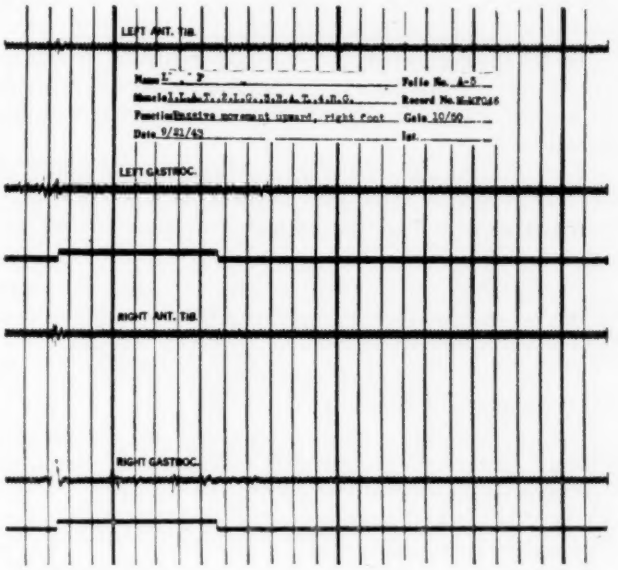


Fig. 12.—Records from same muscles as in figure 9 in a normal person on passive stretching of right gastrocnemius.

stage of infantile paralysis and the least percentage of weakness or paralysis in the neck and back muscles there was no indication that this spasm was the primary cause of the disabilities which create fear of this disease.

From the available conclusive data we establish the following points:

1. In some patients spasticity has been recorded in all muscles which we have investigated.

2. Evidence of spasticity has been recorded from (*a*) weakened muscles, (*b*) the antagonists of weakened

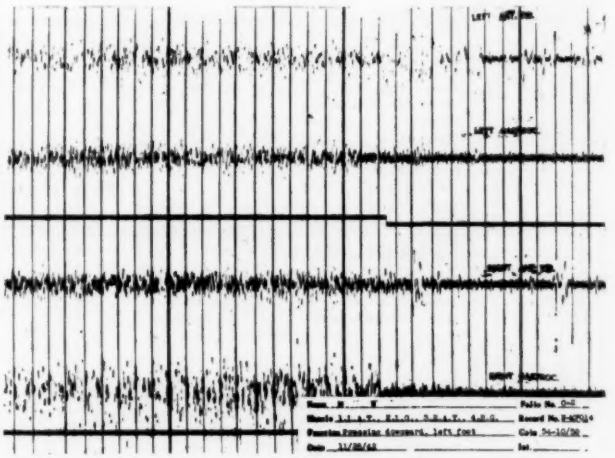


Fig. 13.—Same patient as in figure 9. Action currents of same muscles obtained during voluntary contraction of left gastrocnemius.

muscles and (*c*) muscles which exhibit no clinical or other evidence of weakness.

3. The evidence does not support the view that fibrillation or inflammation of the muscle is responsible for the spasticity.

13. Poliomyelitis: A Survey Made Possible by a Grant from the International Committee for the Study of Infantile Paralysis, Baltimore, Williams & Wilkins Company, 1932, p. 173.

14. Wernstedt, W.: Klinische Studien über die zweite grosse Poliomyelitis-Epidemie in Schweden 1911-1913, Ergebn. d. inn. Med. u. Kinderh. **25**: 705, 1924; Epidemiologische Studien über die zweite grosse Poliomyelitis-Epidemie in Schweden 1911-1913, ibid. **26**: 248, 1924.

15. Lovett, R. W.: Treatment of Infantile Paralysis, ed. 2, Philadelphia, P. Blakiston's Son & Co., 1917, p. 7.

4. On stretching the antagonist of a weakened muscle, the evidence of spasticity in the weakened muscle is frequently greater than the recorded reaction of the muscle in response to voluntary contraction.

5. On stretch reflex of a weakened muscle, spasticity not only is recorded from its antagonist but also is significantly present in records of the corresponding muscles of the opposite extremity.

6. In association with voluntary contraction efforts this spasticity spread was recorded from the same group of muscles as resulted from stimulation by stretch reflex noted in 5.

7. But a muscle which shows no clinical evidence of weakness always produces a stronger voluntary contraction record than the recorded evidence of muscle spasm.

8. There has never been recorded evidence of spasm when a muscle failed to produce a record of reaction to the voluntary movement.

9. Spasticity is a generalized phenomenon in the early stages of infantile paralysis.[16]

10. As prevailing spasm diminished in a weakened muscle, there was recorded evidence of increased strength in the voluntary contraction.

11. The gross initial spasm of neck and back muscles, so characteristic with onset of the acute stage, invariably disappears without evidence of muscle weakness or paralysis.

12. There was no correlation between the degree of spasm and the incidence of muscle weakness or paralysis.

SUMMARY

From action current records made in relation to the study of the neuromuscular reactions of patients in the acute stage of infantile paralysis we conclude that the spine sign is a gross manifestation of the lesser degree of spasm recorded in muscles of normal and subnormal strength.

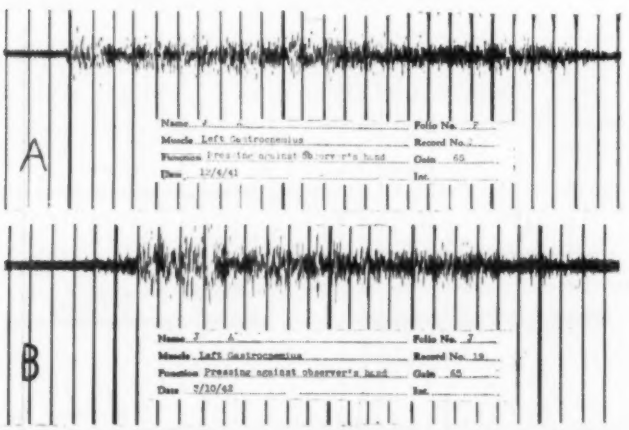


Fig. 14.—Patient with infantile paralysis. *A*, action current record of maximal voluntary contraction of left gastrocnemius taken Dec. 4, 1941. *B*, action current record of maximal voluntary contraction of left gastrocnemius muscle taken March 10, 1942.

In association with the latter, certain functional abnormalities other than muscle weakness were observed in the lower reflex arc. They could be most readily explained in terms of a dysfunction at/or proximal to the dendrites or cell body of the lower motor neuron. This dysfunction resulted in a partial isolation of the lower motor neuron from the inhibition normally induced by other levels through long and short neural pathways. The degree of lower reflex arc isolation thus established and the degree of viability remaining in the lower motor neurons therefore determined the amount of muscle spasm in each instance.

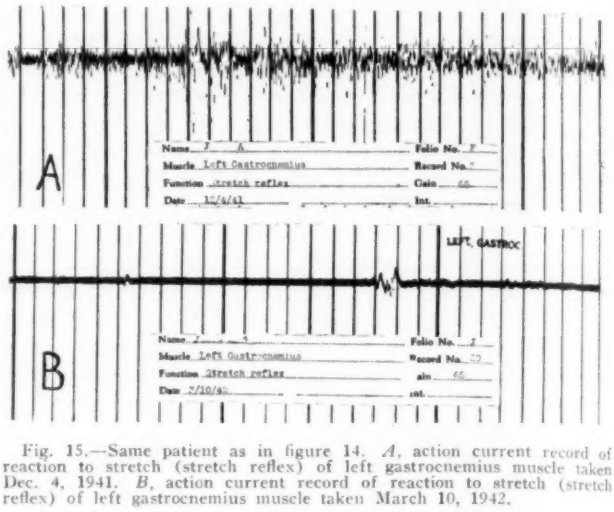


Fig. 15.—Same patient as in figure 14. *A*, action current record of reaction to stretch (stretch reflex) of left gastrocnemius muscle taken Dec. 4, 1941. *B*, action current record of reaction to stretch (stretch reflex) of left gastrocnemius muscle taken March 10, 1942.

Without the involvement of levels proximal to the lower motor neuron there would be no spasm, but the muscle could be either weak or normal, dependent on the number of normal motor neurons innervating the muscle.

If all motor neurons failed to be stimulated by the stretch reflex there would be no reaction to the stretch reflex even though relationships proximal to the dendrites were normal.

Spasticity and weakening are two separate phenomena, each dependent on specific disturbances of functions of the anterior horn cells.[16]

There was every indication that spasm ran its course like other clinical manifestations of the disease.

The relationship between muscle tenderness and muscle spasm has not been clarified by the work thus far done. As in the past, we should continue to differentiate between pain and hyperesthesia from discomfort due to muscle soreness.

We have emphasized the clinical phenomena and the electromyographic evidence which indicates that muscle spasm does not initiate the development of muscle weakness.

16. Bouman, H. D., and Schwartz, R. P.: The Degree, the Extent and the Mechanism of Muscle Spasm in Infantile Paralysis, New York State J. Med. **44**: 147 (Jan. 5) 1944.

Racial Theory.—The assumption that blood is transmitted at birth from parents to progeny and is inherent in the clan or race from the very origin of the racial stock was and is the cause of the blood feuds and wars among clans, tribes and nations and still remains the basis of strife between different nationalities. The racial theory recently revived by Hitler in Germany is reminiscent of the primitive fantastic idea that the blood of a people is inherited from the very first progenitor of that people, or race, and that the blood of certain peoples contains higher spiritual powers than that of neighboring peoples. The conclusion is drawn that the blood of mythological Roman heroes still flows in the veins of the modern Italians, and that the mythical blood of Wotan still circulates in the vessels of the twentieth century Nazis.—Gordon, Benjamin Lee: The Romance of Medicine, Philadelphia, F. A. Davis Company, 1944.

Clinical Notes, Suggestions and New Instruments

BANTI'S SYNDROME APPARENTLY DUE TO INFECTION WITH SCHISTOSOMA MANSONI

THOMAS P. ALMY, M.D., AND J. G. MASON HARPER,
NEW YORK

Infection with the blood fluke Schistosoma mansoni is a highly prevalent disease in Africa, in the northern parts of South America and in the West Indies as far north as Puerto Rico. In the continents of Europe and Asia there is only one small focus, about the city of Aden, Arabia. The disease has apparently never been acquired on the North American continent (fig. 1).

The sharp limits of geographic distribution of the disease are due in part to the complicated life cycle of this flatworm, which requires one of a number of species of snail (of the genera Planorbis and Australorbis) as intermediate host. After development within the snail, the schistosome emerges as a larva, the cercaria, which swims freely near the surface of fresh water streams and ponds and there is capable of penetrating human skin.

Within the human host the growing worms make an extended migration through the blood vessels before reaching their definitive site. They pass in succession through the systemic veins, the right atrium and ventricle, the pulmonary capillaries and the left atrium and ventricle, to be distributed widely in the systemic circulation. Those which reach the mesenteric capillaries pass through into the portal vein, where they reach maturity, mate and then migrate backward in the portal system to reach the venules in the mucosa and submucosa of the colon. This migration is usually not attended by symptoms. When, however, the gravid female worm deposits her eggs in minute venules just beneath the mucosa of the colon, the eggs induce local necrosis, usually with slight hemorrhage, production of small ulcers and symptoms suggestive of mild dysentery. Over a period of many years, during which the disease is clinically silent, a considerable number of ova may be swept by the portal current to the liver, where each produces a minute area of necrosis. These miliary necroses are healed by scarring, and the nearly typical portal cirrhosis may be complicated by splenomegaly, ascites and other sequelae of portal hypertension.

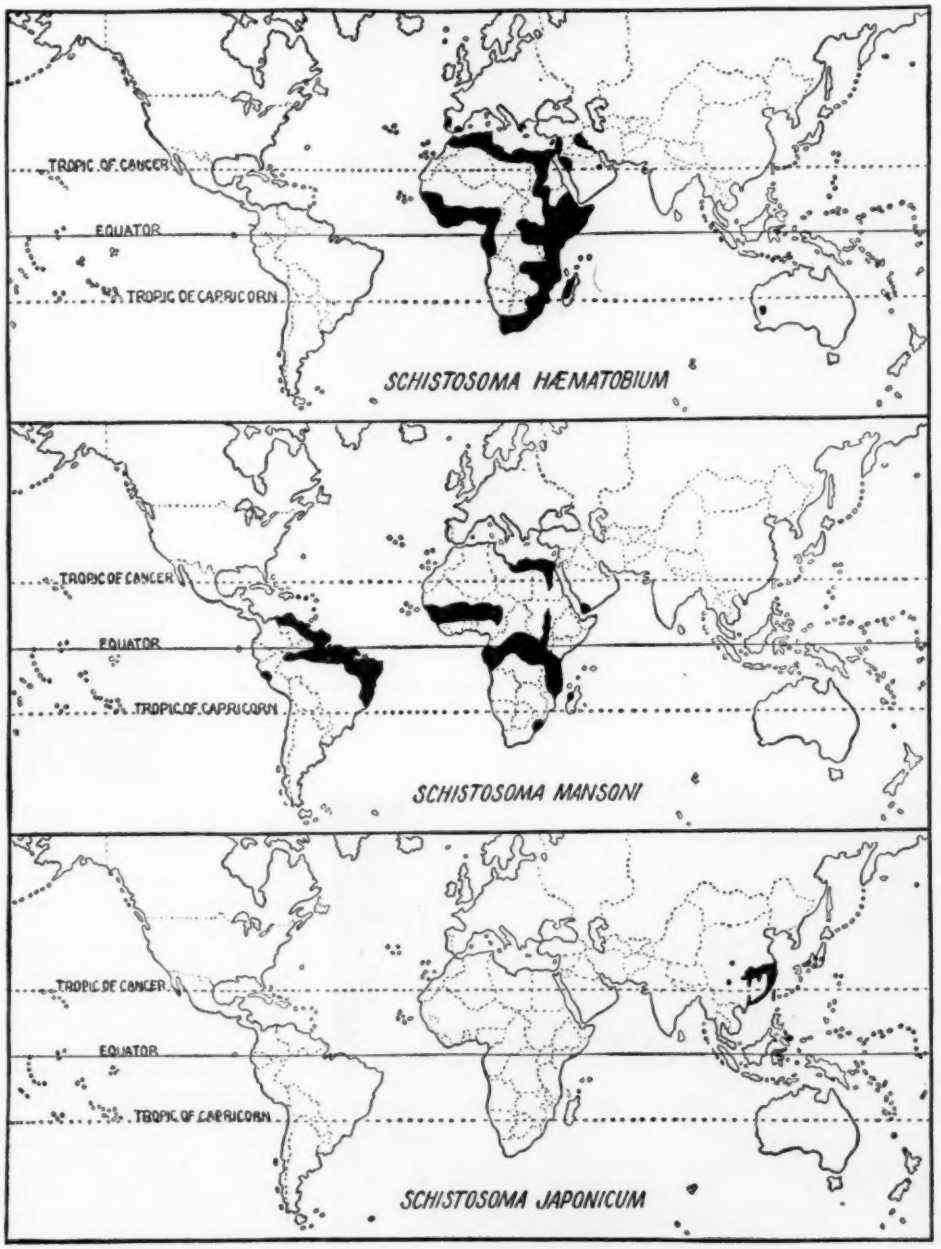


Fig. 1.—The world distribution of schistosomiasis mansoni (from Belding: Textbook of Clinical Parasitology, New York, D. Appleton-Century Company).

In the case herein described, the typical features of Banti's syndrome were apparently due to infection with S. mansoni. A number of such cases in former residents of the endemic areas have been previously identified in the United States by Price [1] and others; yet in the records of our large urban hospital, covering thirty years (1914-1944) and nearly 350,000 admissions, this is the first case of schistosomiasis. It is reported not only for its relative rarity but also as an illustration of the influence of geography on clinical diagnosis.

REPORT OF CASE

This 44 year old Mohammedan Arab was born near Aden, Arabia, and lived there until 1914, when at the age of 15 he joined the British navy. For five years he traveled widely in the navy and then in the merchant marine, only once going ashore, for a few hours, in an area infected with S. mansoni. This was at an Egyptian port, and he had no contact with fresh water while ashore. He landed at Portland, Maine, in 1919 and has remained in the United States since that time.

From the Department of Medicine of New York Hospital and Cornell University Medical College.

Dr. Henry E. Meleney, professor of preventive medicine at New York University, gave helpful suggestions as to diagnosis and therapy. Dr. J. T. Culbertson, assistant professor of bacteriology at the Columbia University College of Physicians and Surgeons, supplied antigen for skin testing.

1. Price, A. S.: Schistosomiasis (S. Mansoni): A Report of 7 Imported Cases, Rev. Gastroenterol. **6**: 115, 1939.

The patient recalled a few episodes of diarrhea with bloody stools at about 14 years of age but remembered no notable pruritus, severe cough or hemoptysis. He had enjoyed excellent health until his present illness. His diet included moderate amounts of fruits and vegetables and small amounts of lean meat. He abstained from alcohol. Two years before admission, when a left inguinal hernioplasty was performed, his spleen was found to be enlarged.

Fig. 2.—Patient's protuberant abdomen, with transverse groove.

The patient had suffered from a chronic dry cough during the winter for many years. Ten months before admission, following a fracture of two ribs in a fall downstairs, he had persistent, more severe coughing, and mild malaise. Three months before admission he became conscious of increasing weakness and weight loss. One month later he first noted heaviness and swelling of the abdomen and swelling of the legs. He became decidedly dyspneic on mild exertion, having to stop after climbing seven steps, but had no orthopnea. He had no nausea or vomiting, no hematemesis or melena, no notable abdominal pain and no jaundice.

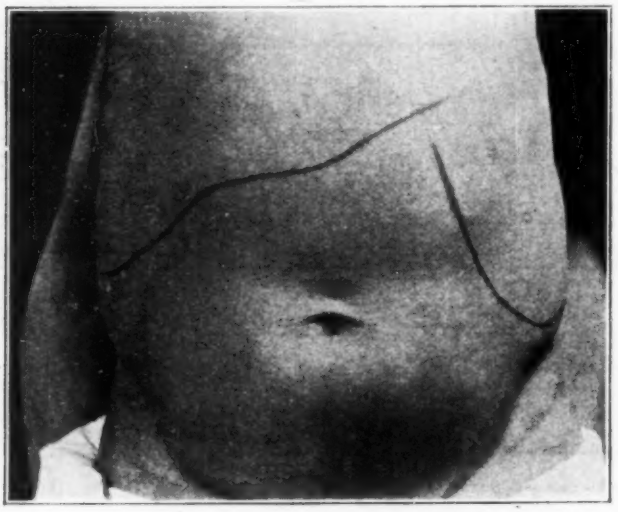


Fig. 3.—Outline of liver and spleen.

The patient was dark skinned and moderately well nourished. His abdomen was protuberant and he was coughing, but he could lie flat without distress. His mucous membranes were pale. The scleras were slightly yellow and displayed bilateral pingueculae. The diaphragms were high, and there were fine moist inspiratory rales at both bases. The heart was not enlarged and was without murmurs. The sharp edge of a hard, nontender liver was felt 7 cm. below the costal margin in the midclavicular line, and the hard, rounded tip of the spleen was felt at the level of the umbilicus. A shallow transverse groove about 3 cm. wide extended across the abdomen at the level of the umbilicus (figs. 2 and 3). There was no fluid. A reducible inguinal hernia was present under an oblique left lower quadrant scar. There was moderate edema of both ankles and pretibial areas.

Examination of the urine showed rare red blood cells and leukocytes. Blood examination revealed hemoglobin 5.2 Gm., erythrocytes 3,600,000, hematocrit 26 per cent, platelets 90,000, reticulocytes 0.5 per cent and leukocytes 4,000 with 6 per cent lymphocytes, 10 per cent monocytes, 12 per cent eosinophils, 2 per cent basophils, 53 per cent mature polymorphonuclears and 17 per cent band forms. The serum protein level was 6.3 to 7.4 per cent with globulin content 3.2 to 4.1 per cent. The cephalin flocculation test was 3 plus and the flocculation test for syphilis (Mazzini) was 3 plus, with the Wassermann reaction negative. The icterus index was 6.0. The prothrombin level (Werner, Brinkhous and Smith method) was 53 per cent and rose only to 55 per cent after 2 mg. of menadione was injected intramuscularly. Chest x-ray and barium enema were negative. A gastrointestinal series disclosed large esophageal varices. The stools were uniformly positive for occult blood.

Fig. 4.—Ovum of S. mansoni (from Giffen in Belding: Textbook of Clinical Parasitology, New York, D. Appleton-Century Company).

The patient was given iron sulfate, elixir of choline chloride, daily intramuscular injections of crude liver extract and a high protein, high carbohydrate diet with supplements of crystalline vitamins. After three weeks his hemoglobin had risen to 11.9 Gm. and his erythrocyte count to 4,900,000, his leukocyte count was unchanged and his eosinophil percentage had fallen to 4. Ankle edema was no longer present and he felt much stronger.

At this time it was suspected that he might have schistosomiasis, and a skin test was performed with antigen obtained from the frog lung fluke (Pneumoneces medioplexus.[2] This was moderately positive. Repeated stool examinations were made by various methods of concentration. On the eleventh such examination, in which the acetic acid-ether method of de Rivas[3]

2. Culbertson, J. T., and Rose, H. M.: Skin Tests in Schistosomiasis with Antigen from Pneumoneces Medioplexus, Am. J. Hyg. **36:** 311, 1942.

3. de Rivas, D.: An Efficient and Rapid Method of Concentration for the Detection of Ova and Cysts of Intestinal Parasites, Am. J. Trop. Med. **8:** 63, 1928.

was used, an ovum of Schistosoma mansoni was found (fig. 4). This observation was repeated in six different preparations from two stools, and the identity of the ova was confirmed by Dr. Ralph W. Nauss, parasitologist to the New York Hospital.

The patient was then treated with fuadin in 6.3 per cent solution, given daily by muscle in dosage increasing from 0.8 cc. to 5 cc. and then maintained at this level for nine additional injections given every other day—a total of 62.6 cc. There were no toxic manifestations and no further change in the symptoms and signs of hepatic disease, or in the blood count, except for a secondary rise of the eosinophil percentage to 25 at the end of treatment. The cephalin flocculation reaction during treatment was 1 plus.

When the patient was last seen, ten weeks after the conclusion of treatment, strength and exercise tolerance had improved. He had climbed ten flights of stairs slowly without stopping. Although ankle edema had disappeared, he had maintained his weight. The liver and spleen were not changed in size. The blood count had remained the same except for a secondary fall of the eosinophil percentage to 7.

COMMENT

In retrospect, there were several reasons for suspecting the parasitic origin of Banti's syndrome in this patient. He had spent the earlier years of his life in a recognized endemic focus of schistosomiasis mansoni. His abdomen presented a shallow transverse groove similar to that described by Faust and Meleny [4] in advanced cases of schistosomiasis japonica. It is thought by them to indicate adhesions of the omentum and mesentery to the abdominal wall, with contraction of scar tissue in these adherent structures. To our knowledge this clinical feature has not previously been described in schistosomiasis mansoni. The patient's blood showed an eosinophilia, which is rarely seen in Banti's syndrome of nonparasitic origin. The diagnosis was strongly suggested by a positive skin reaction to a trematode antigen but could not be considered as established until the ova of S. mansoni, after a prolonged search, were identified in the stool.

The chronicity of this patient's disease was of special interest. It is probable that he was infected at his place of birth, which he left thirty years ago. It is certain that he was infected more than twenty-five years ago, since which time he has lived in the United States.

In the late stage of schistosomiasis which this patient illustrates, treatment with anthelmintic drugs is risky. It is widely held that in the presence of advanced hepatic damage antimony and potassium tartrate is contraindicated and fuadin must be used with caution. Furthermore, the benefit to the patient of such treatment is small, because most of the clinical phenomena are due to irreversible scarring of the liver. The early stages of the disease, those characterized clinically by skin rashes, asthmatic states and protean gastrointestinal symptoms, present greater therapeutic opportunities. In such cases there is usually less difficulty in finding the ova in the stools, but their presence must first be suspected. The variable symptoms and physical signs do not often present a clue and the eosinophilia is inconstant, but any patient may be logically suspected of having schistosomiasis who has exposed himself to fresh water in one of the sharply limited endemic foci of the disease. It is therefore suggested that the first consideration in diagnosis is a geographic one, the fact of exposure to the disease. In the near future, with many Americans returning from endemic foci of schistosomiasis, such thinking may become important in clinical diagnosis.

SUMMARY

Banti's syndrome occurring in a 44 year old Arab was found to be due to schistosomiasis mansoni, although the patient must have acquired this infection more than twenty-five years before the onset of symptoms. The patient was treated with fuadin, with indeterminate results. As it provides a valuable clue in the clinical diagnosis of schistosomiasis mansoni, stress is laid on the limited geographic distribution of endemic foci of this disease.

4. Faust, E. C., and Meleney, H. E.: Studies on Schistosomiasis Japonica, Monographic Series no. 3, Baltimore, American Journal of Hygiene, 1924, p. 222.

Council on Physical Medicine

The Council on Physical Medicine has authorized publication of the following report. HOWARD A. CARTER, *Secretary.*

TELEX NEW SUPER HEARING AID (Model #1550) ACCEPTABLE

Manufacturer: Telex Products Company, Telex Park, Minneapolis.

This is a vacuum tube hearing aid consisting of four midget tubes, a transmitter, a crystal receiver in a flesh colored molded case and a battery unit. Weights and overall dimensions of the various parts of Model #1550 are as follows:

Transmitter, 4 inches by 2¼ inches by ¾ inch, weight with cords 5 ounces.
Receiver, crystal, 1 inch in diameter.
Batteries, weight 11 ounces.
Total weight of the entire instrument is 16 ounces.

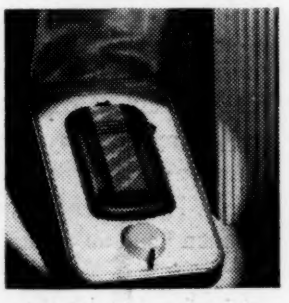
Batteries.—Voltages and current drains are as follows:
A battery, 1.5 volts.
Current drain at ½ volume 110 milliamperes.
Current drain at full volume 110 milliamperes.
B battery, 45 volts.
Current drain at ½ volume 1.5 milliamperes.
Current drain at full volume 1.5 milliamperes.
An additional drain of 0.3 milliampere occurs with loud signal.

Acoustical Gain.—The following data are the average of observations of two trained observers using fitted ear molds seated 5 feet from the loud speaker delivering frequencies of pure sine wave characteristics. (Test made with tone control at "normal white dot position.")

Volume Control Set at	Frequency							
	256	512	1,024	1,448	2,048	2,896	4,096	
½	9	6	8	14	11	10	13	Decibels
¾	15	10	15	19	16	14	18	Decibels

Overall gain for speech 31 decibels. This is an intelligibility speech measurement based on what the patient can understand without the hearing aid and with it.

Physical and Mechanical Features.—The instrument consists of a black plastic molded case of convenient size and pleasing appearance. It is very well made. The electrical assembly has been done in a thoroughly workmanlike manner. There are two controls, one the volume control, a studded disk placed on the top of the instrument. It operates smoothly and easily. A second, the tone control situated on the upper left hand corner of the side, operates in three positions marked by blue, white and red dots. The cord connections are well made and seem to maintain their position without shifting. The battery pack is conventional in type.



Telex Hearing Aid, Model 1550.

Performance.—In this test the instrument submitted performed as represented. At full volume, however, there is definite feedback squeal even with a tight fitting receiver. At full control the instrument performs unusually well. As shown in the graph submitted by the firm, shifts in the low frequency are emphasized very definitely. The booklet of instructions is complete and adequate.

Recommendations.—The aid itself and the descriptive matter which were submitted fulfils the requirements for acceptable hearing aids of the Council on Physical Medicine.

The Council voted to accept the Telex new Super Hearing Aid, Model #1550, for inclusion in its list of accepted devices.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, NOVEMBER 11, 1944

MEDICAL CERTIFICATES AND WAR PRODUCTION

In recent years medical certificates have been required for fuel and food rationing, public health disease prevention programs, food handler control, marriage laws, school regulations and sickness insurance.[1] The good name of the medical profession is sometimes jeopardized by too lenient compliance with appeals for certificates from patients who often have little or no real basis for requesting them. This problem is now especially concerned in present efforts to use limited manpower to its fullest extent in war industries.

Production of munitions would be far from completed even if Germany should capitulate this month. According to War Department announcements, production of heavy trucks, large shells, bombs, rockets, smokeless powder, heavy duty tires, superbombers and large artillery is behind schedule for 1944. These activities must be continued for many months to come if urgent orders from overseas are to be met. The major problem in the production of these critical items is lack of manpower. Lack of labor reserves in many communities, excessive absenteeism and a high rate of labor termination are the controlling factors in producing enough munitions on time. Certain ordnance plants have reported absenteeism amounting to twenty days annually per man [2] and an annual labor turnover of 100 per cent. Many of these absentees and job terminators can be replaced only with the greatest difficulty.

Many observers believe that the principal underlying cause is the too common attitude that the war is almost over. The feeling of urgency is gone. Liberal disability benefits contribute to these delays. Others who drop out for a few days of hunting or to get in the crops cheerfully extend an unjustified absence and cover up by alleging illness on return to work. Job quitters likewise are more common than ever because of their understandable desire to obtain more permanent work before present jobs terminate.

Industry, labor organizations, the War Manpower Commission and other interested agencies have instituted an aggressive plan of action to control the ordinary causes of absenteeism and labor turnovers by giving attention to such factors as housing, transportation, shopping facilities, cafeterias, child care and impressing the workers with the urgency of staying on the job.

Illness, both alleged and real, as a frequent cause of absenteeism and work termination is probably the most difficult problem to control by lay agencies. The government and its contracting agents customarily require medical certificates to cover an absenteeism alleged to illness or a labor termination attributed to reasons of health. The medical profession is then put under pressure by thoughtless persons who see little harm in collecting disability benefits or in obtaining better jobs on pretext of illness. They fail to see the cumulative results of hundreds of thousands of such acts on critical war production.

Responsibility rests squarely on the physician to act as prosecutor, defense attorney and judge before issuing such a certificate. He fails himself, his profession and the war effort if certificates are issued without due cause. The Army [3] is prepared to cooperate closely with physicians in industry in order to accumulate facts about alleged illness of an employee and the possible effects of the working environment on the employees' health. Standard practices for the control of health hazards in war industries are available. The medical records of employees and diagnostic services of these plants are generally available to private physicians in troublesome cases and should be utilized fully.[1]

The medical profession is never out of the public eye. The ability of any group of workers persistently to evade the obligations of their jobs through easy availability of medical certificates must inevitably arouse unfavorable public reaction. The War Participation Committee of the Massachusetts Medical Society has established a system for review of medical certificates in that state [4] worthy of general consideration. Every physician must assure himself that each medical certificate is exactly what it implies—a certified statement of facts based on careful examination and disinterested judgment.

1. McGee, L. C.: Industrial Medical Certification, New England J. Med. **231**: 215 (Aug. 3) 1944.
2. Medical Certification in Industry, editorial, New England J. Med. **231**: 212 (Aug. 3) 1944. Flinn, R. H.: Absenteeism versus Ordnance Production—The Physician's Role, to be published.
3. Cooperation of Plant Physicians with Private Physicians; Industrial Hygiene Information Circular No. 20, Safety and Security Division, Office of the Chief of Ordnance, Army Service Forces, Oct. 29, 1943. Pickard, Karl: The Relation Between the Family Physician and War Industry, New England J. Med. **229**: 714 (Nov. 4) 1943.
4. Massachusetts Medical Society: War Participation Committee, New England J. Med. **231**: 215 (Aug. 3) 1944.

AIR BORNE TUBERCULOSIS

Following development of Topley's [1] method for the study of herd infections, studies of the experimental epidemiology of tuberculosis were begun in the Henry Phipps Institute at the University of Pennsylvania. In the initial experiment Perla [2] exposed normal guinea pigs to tuberculous cage mates which had been previously infected intraperitoneally with highly virulent bovine type tubercle bacilli. The exposed guinea pigs readily contracted tuberculosis. This with few exceptions had the characters of an infection that had entered by way of the digestive tract. Involvement of the mesenteric and cervical lymph nodes was conspicuous in necropsies with an occasional tuberculous ulcer of the ileum. The infection was apparently the result of fecal contamination of the food material. After such intraperitoneal inoculation guinea pigs usually begin the elimination of tubercle bacilli in the feces within a week. There is a rapid increase in the number of tubercle bacilli per fecal bolus during the terminal weeks of the disease.

In the same experiments Perla found that out of 16 normal guinea pigs placed in the same room but not in the same cages with tuberculous animals 2 guinea pigs acquired tuberculosis, presumably as a result of air borne contagion. Each of these cases had the characters of a bronchogenic infection, the dominant lesions being in the lungs and tracheobronchial lymph nodes.

A more detailed study of air borne tuberculosis was therefore undertaken. Twenty-seven cages, each containing 2 normal guinea pigs, were evenly distributed and left undisturbed for several months in a large room harboring about 500 experimental animals, many of them tuberculous. Precautions were taken to rule out non-air borne infection. Lurie [3] found that none of the guinea pigs thus exposed for a period of six months developed tuberculosis. Of the guinea pigs exposed for periods ranging from six to twelve months, 9.1 per cent developed a typical respiratory tract infection. Among those exposed for from twelve to eighteen months 27.7 per cent developed air borne tuberculosis. The morbidity increased to 35.3 per cent among those exposed for periods ranging from eighteen months to two years. Of the 20 guinea pigs that did not contract the disease by the end of two years only 1, or 5 per cent, was subsequently infected. Apparently under his method of exposure animals that do not develop tuberculosis by the end of twenty-four months have a hereditary or acquired resistance to subsequent infection.

Following the demonstration by Wells [4] that pure cultures of tubercle bacilli suspended in air can be killed within three seconds by exposure to ultraviolet light, Lurie [5] and his associates developed a technic for testing the possibility of preventing natural air borne tuberculosis by ultraviolet rays. Two duplicate rooms were prepared. Each room contained a battery of individual cages for normal rabbits with a parallel group of cages for rabbits previously infected intravenously with highly virulent bovine type tubercle bacilli. These infected rabbits were shedding highly virulent tubercle bacilli in the urine. The two batteries were so placed that the natural air currents of the room were from the infected to the exposed rabbits. In the test room the space between the donor and recipient cages was flooded by ultraviolet light. No lamp was installed in the control room.

The recipients in each room were litter mates of the same highly inbred, genetically uniform rabbits. Three genetic strains were used: a hereditarily highly resistant rabbit family and two families of low hereditary resistance. Every two weeks each of the exposed rabbits was tested for acquired skin sensitivity, and every four weeks it was x-rayed. At the end of fifteen months all surviving exposed animals were killed and carefully examined, guinea pig inoculation being resorted to in case of the least doubt.

In a typical experiment (1942-43 series), 8 hereditarily resistant rabbits and 7 rabbits of the susceptible families were placed in each room. Within six to twelve months all exposed rabbits in the control room had developed a high degree of skin sensitivity. Twelve of the 15 had developed from 2 plus to 4 plus tuberculosis, of which 9 died. In the irradiated room no rabbit developed a positive skin reaction by the end of twelve months. But 1 ultraviolet room rabbit developed a questionable pulmonary lesion. From this lesion tubercle bacilli were isolated by guinea pig test.

Summarizing the results of three years' research, Lurie concludes that under the conditions of their experiments ultraviolet rays of high intensity completely protect all rabbits, whether of high or low natural resistance, from an air borne contagion so severe as to be fatal to the great majority of rabbits of the same genetic constitution if not protected by such radiation. The protected animals do not develop tuberculin sensitivity. With irradiation of low intensity, rabbits of high natural resistance are completely protected from acquiring demonstrable tuberculosis, though they do acquire tuberculin sensitivity. Low intensity irradiation, however, does not protect all rabbits of low natural resistance from acquiring lethal tuberculosis. From these encouraging results Lurie believes that "it is probable that ultraviolet radiation may control air borne contagion of human tuberculosis."

1. Topley, W. W. C.: J. Hyg. **19:** 350, 1920-1921.
2. Perla, D.: J. Exper. Med. **45:** 209, 1927.
3. Lurie, M. B.: J. Exper. Med.: **51:** 743, 1930.
4. Wells, W. F., and Lurie, M. B.: Am. J. Hyg. **34:** 21 (sec. B) 1941.
5. Lurie, M. B.: J. Exper. Med. **79:** 559 (June) 1944.

Current Comment

GRADUATE EDUCATION OF PHYSICIAN VETERANS

Elsewhere in this issue, page 709, appears a report on the graduate education of physician veterans which carries information of the greatest importance to all physicians now serving with the armed forces. Preliminary reports on the results of the questionnaire sent by the Committee on Postwar Medical Service to all physicians in the armed forces indicate that the majority of physicians wish graduate education, including short and long courses, in the postwar period. Under existing legislation physicians, like other veterans, are entitled to payment of tuition and also to cost of subsistence when engaged in such courses, subject to limitations which depend on the duration of the service and similar factors. A conference held by representatives of the Committee on Postwar Medical Service with representatives of the Veterans Administration and of the Vocational Rehabilitation and Education Service brought out the facts clearly.

GENERAL MEDICAL COVERAGE FOR INDUSTRIAL EMPLOYEES

Recently in THE JOURNAL a series of articles [1] was published describing some of the variations in approach which representative industries have made to the problem of general medical coverage for their member-employees. The Council on Industrial Health, in recognition of this trend, has adopted a statement of policy which should be helpful to physicians and medical societies faced with these developments. This statement, as approved by the Board of Trustees of the American Medical Association, is as follows:

Pressure is being placed on industry by management and by labor to extend the health services for which it is responsible. It has been recognized that industry has certain responsibilities in providing medical care for occupational injuries and diseases. These responsibilities have been extended to include various services in the field of preventive medicine. It is now proposed that industry provide over-all medical care for employees and their dependents, the term medical being used in a broad sense to include diagnosis and treatment in various special fields. The Council on Industrial Health believes that a statement along the following lines bearing the stamp of approval of the American Medical Association will be of assistance to physicians who are now confronted with this situation in many areas:

1. The principles on which medical care plans should be based have been defined by the House of Delegates of the American Medical Association. In developing medical care plans, industry should be in agreement with the local county medical society as to the conformity of such plans with these established principles. Plans of this nature should include provision for health maintenance programs.

2. Because of the essential medical nature of such plans, their policies should be directed and the medical phases should be controlled by the medical departments of industry.

3. The attention of industrial management should be directed to the place of the physician in industrial organization. The expanding importance of health activities in industry demands that the physician be responsible directly to top management and that activities relating to health be centered in and directed through the medical department.

1. Adams, J. M.: Stanocola Medical Care Plan, J. A. M. A. **126:** 333 (Oct. 7) 1944. Bloom, M. S.: Variations in Current Industrial Medical Service Plans, ibid, p. 335. Garfield, Sidney R.: Health Plan Principles in the Kaiser Industries, p. 337. Jones, E. M.: The Endicott-Johnson Plan, p. 339. McCann, James C.: Medical Society Prepayment Programs. Lessons Learned from Experience in Massachusetts, p. 341. Wittmer, John J.: Variations in Current Industrial Medical Service Plans, p. 344.

THE DALLAS VENEREAL DISEASE CONTROL PROGRAM

A Venereal Disease Control and Educational Program was organized in Dallas, Texas, in the summer of 1943 at the suggestion of the commanding officers of the armed forces in that area. A report by the Dallas Venereal Disease Educational Committee [1] was issued on July 1, 1944. The Dallas program differs from the Chicago program [2] in that the Chicago program is a cooperative one in which the United States government, the state of Illinois and the city of Chicago are primarily concerned, whereas the Dallas program was carried out by two local committees, one on venereal disease control and the other on venereal disease education. The report outlines the procedures and describes the results. Pictures by the United States Army Signal Corps show the participation by community agencies and the public in the program. A typical double page spread layout shows a street corner with curb billboard, another billboard at factory gates, posters in a public waiting room, information on the inside of a washroom door, windshield stickers, car cards, a clinic scene, a dinner meeting and informational posters at soda fountains. Stickers were placed in juke boxes and elaborate exhibits displayed in public places. Films were used; these were seen by more than ninety-four thousand persons during the campaign. Fifty thousand water bills were stuffed with folders featuring venereal disease information. An active speakers' bureau, in which forty-four physicians participated, scheduled as high as three and four talks a day. Newspaper space was used to a total of 1,412 inches of paid advertising at a special rate lower than the regular advertising rate. In this program the people of Dallas got to work. The entire expense of the campaign was just over $3,000, but this does not count the value of volunteer labor or the expense of materials received gratis from official agencies, especially the state health department. Results are indicated as follows: "A recent report by the medical director of the Eighth Service Command showed that the average rate of infection among military personnel for the three month period ending June 1, 1944 was 10.5 cases per week, a drop of more than 80 per cent as compared with the average weekly rate at the beginning of the campaign." A year is a short time in public health history. Doubtless this campaign, if continued, will show even greater results not only in the military but in the civilian population.

1. Venereal Disease Control and Education in Dallas, Texas, 1943-1944, a report by the Dallas Venereal Disease Educational Committee, July 1, 1944.

2. Progress Report Chicago Venereal Disease Control Program 1942-1943, Board of Health, Chicago.

MEDICINE AND THE WAR

POSTWAR PLANNING

GRADUATE EDUCATION OF PHYSICIAN VETERANS

Report of the Subcommittee of the Committee on Postwar Medical Service

Dr. Frederick A. Coller, Dr. Walter Palmer and Father Alphonse M. Schwitalla, three members of the Subcommittee on Postwar Education of Physician Veterans, were accorded interviews with officials of the Veterans Administration on the afternoon of October 16. The other two members of the committee, Dr. Victor Johnson and Lieut. Col. Harold C. Lueth, found it impossible to attend.

The subcommittee called first on Dr. Charles M. Griffith in the office of the Medical Director, Veterans Administration Building, and after an exchange of courtesies was escorted by him to the office of Mr. Harold V. Stirling, Director, Vocational Rehabilitation and Education Service. Dr. Griffith explained that Mr. Stirling was in charge of the administration of title II of education of veterans of Public Law 346, 78th Congress, known as the "Servicemen's Readjustment Act of 1944" (the G. I. bill), and Public Law 16 was Mr. Stirling's responsibility.

Dr. Griffith explained that after the committee's interview with Mr. Stirling to learn from him the present status of Public Law 346 and its application to the physician veterans, he would discuss with the committee further the content and administration of the educational program itself which the Veterans Administration has projected or intends to project for the returning physicians.

I. ELIGIBILITY OF INSTITUTIONS

Mr. Stirling suggested that the committee discuss first the eligibility of institutions for recognition as educational centers in which veteran physicians might receive such educational benefits as are provided for under the law. He turned to section 400, part VIII, paragraph 4, and called attention to the fact that it is incumbent upon the administrator to

> secure from the appropriate agency of each state a list of the educational and training institutions (including industrial establishments), within such jurisdiction, which are qualified and equipped to furnish education or training (including apprenticeship and refresher or retraining), which institutions, together with such additional ones as may be recognized and approved by the administrator, shall be deemed qualified and approved to furnish education or training to such persons as shall enroll under this part.

Mr. Stirling noted that the law distinguishes between institutions (giving training) "and establishments furnishing apprentice training on the job" (see paragraph 5). The institutions in which discharged physicians would receive their postdemobilization education, such as the hospitals, will, of course, qualify as institutions and will not be considered merely as "establishments furnishing apprentice training on the job."

To qualify as "institutions," the schools of medicine and the hospitals in which the returning physician will be further educated will have to appear by name on a list of educational and training institutions furnished by the appropriate agency of each state to the administrator. The administrator is given authority by the law to "recognize and approve" institutions on his own initiative. Obviously, however, the administrator will not undertake as a rule an approving or accrediting program and will rely on such lists as are furnished him by the appropriate agency of each state.

As far as medical education is concerned, there is very little difficulty about the schools of medicine,[1] since most, if not all, of the states would readily submit the names of schools recognized by the Council on Medical Education and Hospitals of the American Medical Association. Much greater difficulty, however, will be found in supplying to the administrator a list of the recognized and approved hospitals, and a decision will have to be made concerning the list which all will agree will be the proper list to submit to the administrator. Mr. Stirling is of the opinion that it might be well if the administrator's office send to the governors of the various states such lists of institutions, schools and hospitals as are recognized and approved by appropriate agencies with the request to the governor to indicate his approval or disapproval of these lists as appropriate educational centers for the further education of the physician veterans under the program. Naturally, there are other outstanding problems concerning the eligibility of institutions which will need further discussion.

The important conclusion, however, is that in Mr. Stirling's opinion the schools and hospitals can be regarded as institutions within the intent and scope of the Servicemen's Readjustment Act of 1944, provided such institutions qualify under the provisions of paragraph 4, part VIII, title II, Public Law 346.

II. ELIGIBILITY OF INDIVIDUALS

"Any person who served in the active military or naval service on or after Sept. 16, 1940 and prior to the termination of the present war and who shall have been discharged . . . and whose education or training was impeded, delayed, interrupted or interfered with by reason of his entrance into the service . . . and who either shall have served ninety days or more . . . shall be eligible for and entitled to receive education or training under this part" (section 400, part VIII, paragraph 1). A number of provisions and limitations are included in the unquoted section of this paragraph but, in general, the substance of the provision is accurately given. Discharged servicemen under 25 years of age at the time they entered the service are assumed to have had their education impeded or delayed, while those 25 years of age or over at the time they entered the service will be expected to supply evidence that such a delay or obstacle to their education occurred.

With reference to the section just quoted, Mr. Stirling was of the opinion that any physician who is now in any of the branches of the service and has been on active duty for more than ninety days will be eligible for any of the benefits provided by the law. Even those who are more than 25 years old and desire refresher or other courses will no doubt be considered eligible even though they may have entered the Army at a time when their education might have been assumed as completed, since the law in providing refresher and retraining courses is naturally to be interpreted in a liberal spirit.

Any person who has been in active service for three months will be entitled to a period of one year of education or for such lesser time "as may be required for the course of instruction chosen by him." Those servicemen who have been in the service for more than the minimum period of three months may receive additional periods of education or training, the period "not to exceed the time such person was in active service on or after Sept. 16, 1940 and before the termination of the war." Periods during which a serviceman was receiving his education under the auspices of the Army or Navy while on active duty cannot be counted toward time credit for a prolongation of the educational period. The committee asked Mr. Stirling to apply this to the ordinary clinical residency. It was explained to him that the residencies in our hospitals, for example, were one, two or three years or more in length. He replied that:

Those in service three months are entitled to one year further education;

Those in service twelve months are entitled to two years further education;

Those in service twenty-four months are entitled to three years further education.

1. The problem of the state approved but not nationally approved schools of medicine was not touched on in this conference.

Intermediate periods of service entitle the serviceman to intermediarily long periods of education; thus if a serviceman has served six months he is entitled to eighteen months of further education.

III. TUITION AND FEE BENEFITS

The law provides that the administrator shall pay to the educational or training institution the tuition costs and fees as are customarily charged and may also pay for books, supplies and equipment and other necessary expenses, provided the payments with respect to any one person should not exceed $500 for an ordinary school year. These payments are not to be paid to "establishments furnishing apprentice training on the job." The law provides that if the institution has no established tuition fee or if the administrator deems the established tuition fee to be inadequate compensation, the administrator is authorized to provide for the payment. Again, however, with the $500 ordinary school year limitation.

Applying these provisions of the law to the case of residencies in our hospitals and courses in our universities for our physician veterans, Mr. Stirling was of the opinion that there would be no difficulty about the payment of tuition and fees by the administrator for those physician veterans who elect courses in schools of medicine or for those who elect clinical courses in university hospitals where a formal program has been inaugurated. He was also of the opinion however that, provided the hospital can be certified to the administrator by the appropriate state agency as a competent educational and training institution, the administrator may fix the tuition to be paid to such an institution under the provisions of the law (see last sentence, section 400, title VIII, paragraph 5).

The arrangements heretofore in use in hospitals were explained to Mr. Stirling, it being pointed out that the hospital, generally speaking, not only did not charge tuition but actually offered the resident a stipend. He replied by saying that in his opinion if the hospital is certified as a bona fide educational institution the tuition for the physician veterans can be paid to that hospital even though the hospital still continues to pay a stipend to the veteran.

IV. SUBSISTENCE BENEFITS

The law provides further that on application to the administrator the person taking courses shall be paid a subsistence allowance of $50 per month if without a dependent or dependents or $75 per month if he has a dependent or dependents.

This provision again, Mr. Stirling believes, is applicable to the physician veterans who choose to take courses in medical schools or hospitals. Mr. Stirling is of the opinion, furthermore, that the subsistence benefit may be paid the physician veteran even if he receives a stipend from the hospital, since in some cases the physician veteran will undoubtedly live outside the hospital and in many cases there will be a noticeable disproportion between the stipend paid by the hospitals and the salary level of the physician veteran before his discharge. It was pointed out, furthermore, that the subsistence benefit includes "regular holidays and leave not exceeding thirty days in a calendar year." There may still be some question whether the provisions of the law pertaining to attendance in courses on a part time basis and a corresponding part compensation for productive labor are applicable here but there seems no reason to anticipate an adverse ruling on this point. Furthermore, it should be noted that the administration has thus far defined a school year as thirty weeks for the purpose of administering the law; hence the tuition allowance of $500 maximum can be made payable to the institution every thirty weeks if that is the interpretation and regulation under which the educational institution is operating. The subsistence benefit is not affected by the length of the school year.

V. STATUS OF THE VETERANS ADMINISTRATION PHYSICIANS

The provisions of the Readjustment Act as summarized apply, of course, to all institutions in which the physician veterans will expect to take courses; hence the committee asked Dr. Griffith whether, in case the Veterans Administration opens its own hospitals to the physician veterans for refresher and retraining courses and for residencies, just what the status of these physicians would be.

Dr. Griffith explained that this is one of the outstanding problems which the Veterans Administration must face. At the present time the Veterans Administration physicians under a civil service status are full time appointees and at present there is no provision in the organization for residents. A graduate of a school of medicine who has had a good education, if appointed, enters the Veterans Service at a salary of $3,200. After about eighteen months his salary is approximately $3,800, while after ten to fifteen years he may reach a base salary of $6,400. Clearly, the physician veterans if appointed to such positions would be in a particularly fortunate position, at least with reference to salaries, but obviously such an arrangement is not the one which is contemplated by the Servicemen's Readjustment Act. Just how this problem will be solved if the facilities of the Veterans Administration are offered for this educational program is not clear at the present time. A medical corps within the Veterans Administration would obviously solve the problem.

It is expected that within approximately five years the Veterans Administration will have 300,000 beds in about 150 institutions. At present the administration has about 1,800 physicians, approximately one fifth of whom are at the higher salary levels. This will give some indication of what might be expected in the future, but the Vocational Rehabilitation Program of the Veterans Administration will require many more physicians than would be indicated by the present physician to patient ratio. It would seem, briefly, that it is highly desirable to establish an educational program within the Veterans Administration for the physician veterans so that these veterans may have the benefit of the unquestionably large and desirable facilities of the veterans' hospitals and, secondly, that the administration must make provision for a much larger physician personnel.

VI. MEDICAL SERVICES OF THE VETERANS ADMINISTRATION

The committee was given the benefit of a further interview with Dr. Charles M. Griffith, Medical Director, and with Col. Hugo Mella, M. C., Assistant Medical Director, in charge of Postgraduate Instruction and Medical Research. Dr. Griffith explained the structure of the Veterans Administration, emphasizing the extent and variety of the medical responsibilities of the administration. The medical director is responsible to the administrator through an assistant administrator. He has a number of assistant medical directors (at present five) who are in charge of various divisions, namely, general medicine and surgery, neuropsychiatry, outpatient and authorization, tuberculosis and, lastly, postgraduate instruction and medical research. There are a medical executive officer and a medical consultant. The only medical activity of the administration which does not fall within the responsibility of the medical director is the medicolegal activity, namely, the activity of physicians on various boards dealing with claims, adjustments and insurance.

Dr. Griffith and Colonel Mella then went on to speak of the various kinds of physician veterans in whom the Veterans Administration is interested. The first class is the discharged physician who qualifies for further education under the G. I. bill and who is adequately taken care of. The second group is the group of those who would like to qualify for an educational program in the Veterans Administration itself. The status of this group is not clear at the present time, since provisions must still be made for them. A third group of physicians might be those who would be discharged on the basis of physical disabilities and for whom both educational and other provisions will have to be made. If it was possible for the Veterans Administration to organize its own board and its own medical corps, many of the present difficulties with reference to medical care within the Veterans Administration could be promptly removed. At present the Veterans Administration has had assigned to it a number of physicians by the Surgeon General. Colonel Mella stated, after being asked, that for the next two years he estimates that in the veterans' hospitals there should be place for approximately 250 residents. He estimates, furthermore, that 50 per cent of these could be employed in surgical residencies, 35 per cent in psychiatric and internal medicine resi-

dencies and 15 per cent in tuberculosis residencies. He called attention to the great difficulty under which the administration labors in developing an educational program arising from the fact that neither psychiatric nor tuberculosis hospitals have thus far been approved for residencies. By whom and when will such approval take place and what agency will undertake the definition of staff membership qualifications?

It is obvious that the Veterans Administration has given considerable thought to the organization and content of an educational program for physician veterans. Colonel Mella is studying the outline for graduate instruction in surgery as given to him by the College of Surgeons. He and his assistants are planning, moreover, to organize an appropriate committee in each of the veterans' hospitals in which residents are to be instructed which will assume responsibility for the educational program, the committee to consist of the chief medical officer, the clinical director and the chiefs of the various services. The administrator has recently approved functional charts of organization for the various classes of facilities of the Veterans Administration, and, with such clear definitions as have been given, it should be a relatively simple matter to integrate with the existing functions the further function of education for our returning physician veterans.

FREDERICK A. COLLER, M.D., Chairman.
WALTER PALMER, M.D.
ALPHONSE M. SCHWITALLA, S.J., Secretary.

ARMY

MEDICAL FIELD SERVICE SCHOOL AT CARLISLE BARRACKS

When a young man is enrolled in the medical department of the Army he is likely to be sent in the vast majority of cases to the Medical Field Service School at Carlisle Barracks, Pennsylvania. The school is located in Cumberland County at the foot of the Appalachian Mountains. It is about 18 miles from Harrisburg. The primary purpose of this school is instruction and training of officers of the medical department—essentially what is called indoctrination. The needs of war have brought about a condensation of the usual five months course to a six weeks period. In this time the student officer is instructed in tactics, the operation of medical units, preventive medicine, field sanitation and the application of medicine and surgery in the field. Included are practical demonstrations and participation in maneuvers. An officer candidate school for enlisted men of the medical department is carried on simultaneously.

Physical conditioning is an important part of the work and is intended to develop physical stamina, agility and coordination. This involves the usual marching, physical drill and the handling of litters carrying wounded. One area is set apart for actual demonstration of field sanitation. This area occupies 8 acres of ground. Here are shown all the different technics for disposing of kitchen waste and human waste, for the control of lice, flies, mosquitoes and other insects, rat proofing, the preparation of water for use in the field, the disposal of sewage, the setting up of baths and many other sanitary measures. In the course of this work many new processes have been developed and are widely used in our armed forces.

In the mountain area closely associated with Carlisle Barracks, about 7 miles from the post, the medical officer learns how to read maps, set up medical installations for the transportation of the wounded and perform actually in the field many of the life saving procedures that he will have to do once he is in active service at the front. Furthermore, there is an infiltration course used to condition students mentally to the conditions of combat. Here the student gets out of a trench, crawls 80 yards, negotiates barbed wire obstacles, enters other trenches, and this with machine guns firing ammunition 36 inches overhead.

MEDICAL EQUIPMENT LABORATORY

The Medical Department Equipment Laboratory was established in 1920 by the Surgeon General of the U. S. Army and represents at this time one of the most fascinating museums of medical equipment to be found anywhere. Probably it is the only institution of its kind in the world. Here the visitors can see complete outfits of medical supplies for the operating room, the laboratory and the x-ray unit of the Japanese, Italian, German, French and other armies. Here are experiments in the development of light weight litters, operating units to be used in the field, motorized medical devices and innumerable other forms of apparatus. Here are models of ambulance trains and ambulance ships going back to the time of the Civil War and coming up to the latest of the devices available today. The dental equipment parallels that of medicine. When a need occurs anywhere among our troops in the air, on land or on the sea, a message sent to the Medical Department Equipment Laboratory puts the investigators to work and in the vast majority of instances they have been able to meet every request, showing ingenuity that taxes the imagination. This laboratory is under the direction of Col. E. D. Quinnell, and any physician who has an opportunity to visit it and to study its content under the tutelage of Colonel Quinnell will be exceedingly well rewarded for his time and interest.

The textbook of Carlisle Barracks is the Instructors' Guide, a comprehensive work on the service of the medical department in war, written especially for the condensed course now being given. Here are all the details of defense against chemical warfare, mechanized warfare, air and parachute attack, hand to hand combat and what not. The significance of this instruction and training for the good of the nation and for the health and fitness of our troops is so great that one may anticipate a time in the postwar period when the six weeks condensed course may well be part of every medical curriculum.

NONCOMBAT DUTY TO SOLE SURVIVING SON IF TWO OR MORE BROTHERS HAVE BEEN KILLED

In recognition of the sacrifice and contribution made by a family which has lost two or more sons and has only one surviving, the War Department has approved a policy of returning to or retaining in the continental United States the sole surviving son of a family in cases in which two or more sons have been lost, except when the surviving son is engaged in nonhazardous duty overseas.

Sympathetic consideration will be given to every application in cases of families who have lost two or more sons and have only one surviving for return of the survivor to this country for duty here or for discharge from the Army, if the circumstances warrant. However, each case will be decided on its individual merits. In all cases of extreme hardship arising from family circumstances the Army has in the past cooperated to provide relief from active duty or discharge if the complaint has been found to have merit on investigation. The plan of removing men from the hazards of combat activity is an extension of this policy.

HOSPITAL NAMED IN HONOR OF COLONEL MADIGAN

The Madigan General Hospital, Fort Lewis, Washington, has been named in honor of the late Col. Patrick Sarsfield Madigan for his long and faithful service in the Army Medical Corps. At the time of Dr. Madigan's death in May of this year he was chief surgeon at Fort Belvoir, Virginia, Station Hospital. He graduated from Georgetown University School of Medicine, Washington, D. C., in 1912. Dr. Madigan began his army service in 1917, entering the Medical Corps and serving during the last war in France with the 7th Division. He was stationed in the Philippine Islands for two years and served four years in the Panama Canal Zone. In 1940 he was appointed medical adviser to the Surgeon General and the Adjutant General of the Army. Before going to Fort Belvoir in February he was commanding officer of Camp Lee, Virginia, Station Hospital. Col. A. P. Clark is commanding officer at the Madigan General Hospital.

MAJOR CLINTON S. MAUPIN A JAPANESE PRISONER

Major Clinton S. Maupin, formerly of Waurika, Okla., who has been a prisoner of war in Japanese prison Camp No. 1, Cabanatuan, Philippines, since he was captured on Bataan, recently sent a card stating that he is in excellent health and is looking forward to seeing his family again soon. Dr. Maupin graduated from the University of Oklahoma School of Medicine, Oklahoma City, in 1934 and entered the service Nov. 8, 1940.

ARMY AWARDS AND COMMENDATIONS

Captain John J. McCallig

Capt. John J. McCallig, formerly of Rochester, Minn., has been awarded the Purple Heart. Dr. McCallig was in the invasion on D day as a first surgeon, and three days later, at night, his hip was struck by an E boat torpedo in the Channel. His clothing and life-belt were torn from him by the blast, and he swam for an hour or more in the icy water until he found a small raft, from which, two hours later, a British destroyer rescued him. Dr. McCallig graduated from the University of Oregon Medical School, Portland, in 1937 and entered the service July 12, 1942.

Major Paul L. Dent

Presentation of the Bronze Star Medal for meritorious service in combat was made recently to Major Paul L. Dent, formerly of Louisville, Ky., by Brig. Gen. Ralph H. Goldthwaite, commanding general, Army and Navy General Hospital, Hot Springs National Park, Ark. Dr. Dent, serving as operating surgeon in charge of a general surgical team in the Tunisian campaign, performed major surgery on battle casualties close to the front lines. His force and guidance in the speedy and successful care of seriously wounded battle casualties, despite serious difficulties and handicaps, contributed to the saving of the lives of several hundred men at his advance station. For his vital performance and pioneering the principles on which major surgery in the forward areas is now based, Dr. Dent was awarded the Bronze Star Medal. Dr. Dent graduated from the Medical College of Virginia, Richmond, in 1931 and entered the service in July 1942.

MISCELLANEOUS

CIVILIAN MEDICAL ATTENDANCE

Circular No. 214, recently issued by the headquarters of the Sixth Service Command, states that civilian medical attendance at public expense is authorized for military personnel while on a duty status or when absent on authorized leave, sick leave, furlough or pass only when the required attendance cannot be provided from available facilities of the Army or other federal agency. Other federal agencies include hospitals of the U. S. Navy, U. S. Public Health Service, Veterans Administration facilities and Indian hospitals. Prior authority for treatment of patients in these hospitals is not required.

Commanding officers sending patients to hospitals of other government agencies will send at the same time a letter requesting treatment of the patient, this letter to be signed by the responsible officer, and to give the information required by paragraph 4 c (1) AR 40-525. If the patient is admitted to the hospital while on pass, leave or furlough, or while absent without official leave, the responsible officer, on notice from the hospital of admission of patient, will write a request for treatment, covering information outlined in paragraph 4 c (2) AR 40-505.

WARTIME GRADUATE MEDICAL MEETINGS

The following subjects and speakers for Wartime Graduate Medical Meetings have just been announced:

U. S. Naval Hospital, Philadelphia: Neoplasms in Service Personnel, Dr. Stanley P. Reimann, November 17; Practical Aspects of Psychosomatic Medicine, Dr. Louis J. Karnosh, November 28.

Bruns General Hospital, Santa Fe, N. M.: Address of Welcome, Brig. Gen. Larry B. McAfee. Symposium on Coccidioidomycosis: Introduction of subject, Major Samuel I. Kooperstein. Speakers, Dr. C. E. Smith, Major Norman Nixon, Lieut. Col. Brian Blades, November 16. Symposium on the Repair of Soft Tissue and Bone Defects of the Extremities: Introduction of subject, Lieut. Col. John D. Koucky. Speakers, Dr. Edward L. Compere, Dr. Earl C. Padgett, Major C. L. Robertson, Lieut. Col. W. W. Schuessler, November 16. Symposium on the Pathology of Tuberculosis: Introduction of subject, Lieut. Col. George J. Kastlin. Speakers, Col. Edmond R. Long and Col. Hugh Mahon, November 17. Symposium on Pulmonary Tuberculosis: Introduction of subject, Major George C. Owen. Speakers, Col. Edmond R. Long, Lieut. Col. Brian Blades, Col. Hugh Mahon, Capt. William H. Roper, November 17. Symposium on Bone and Joint Tuberculosis: Introduction of subject, Major Frederick J. Fischer. Speakers, Dr. Edward L. Compere, Dr. Earl C. Padgett, Col. Edmond R. Long and Col. Hugh Mahon, November 18. Symposium on Chest Surgery: Introduction of subject, Lieut. Col. John D. Koucky. Speakers, Lieut. Col. Brian Blades and other speakers not yet announced, November 18.

U. S. Naval Hospital, Long Beach, Calif.: Some Phases of Peripheral Nerve Surgery, Dr. R. B. Raney, November 18.

Mayo General Hospital, Galesburg, Ill.: Conditions Affecting Glucose Metabolism, Dr. Arthur R. Colwell, November 15.

Camp Ellis, Camp Ellis, Illinois: Dermatologic Diseases, Drs. Stephen Rothman, Robert M. Craig and George X. Schwemlein, November 15.

Chanute Field, Rantoul, Ill.: Low Back Pain, Drs. Fremont Chandler and Adrien H. P. E. Ver Brugghen, November 15.

PRISONERS OF WAR SERVICES

Through the cooperation of the American Red Cross, special optical, dental and orthopedic services are being provided for American prisoners of war. The American Red Cross reports that in all European prisoner camps the detaining power provides eye examination service. Prescriptions prepared by the camp optometrist are sent to Geneva, where a large pool of lenses has been established. When Geneva cannot fill the prescription it is filled elsewhere in Switzerland.

It was also reported that each camp usually has its own dentists: a German, American or another Allied dentist who is a prisoner. To meet shortages, dental supplies valued at about $12,000 have been shipped to the International Committee of the Red Cross. When special dental treatment is needed it is paid for out of a revolving fund.

Temporary replacements are provided by their captors for prisoners who have lost a leg or an arm. The British and American Red Cross societies follow through by providing the best permanent mechanical limbs as soon as possible. To accomplish this a Swiss orthopedic mission visits all camps and measures the prisoners for artificial limbs. These are constructed in Switzerland for American prisoners at the expense of the American Red Cross.

WAXED PAPER FROM CIGARET CARTONS USED AS SURGICAL DRESSINGS

Capt. Richard A. Twyman, formerly of Rochester, Minn., discovered that waxed paper from the wrappers of cigaret cartons can be used for surgical dressings when the usual nonadherent substances are unavailable. Holes are punched at quarter-inch intervals to permit drainage and irrigation. The waxed papers are washed with soap and water, placed in a shallow pan, wrapped like other surgical dressings and then sterilized in the usual manner. Dr. Twyman graduated from Northwestern University Medical School, Chicago, in 1938 and entered the service June 19, 1943.

ORGANIZATION SECTION

Official Notes

CHANGE 1945 ANNUAL MEETING PLACE

The House of Delegates of the American Medical Association at the annual session held in 1942 selected New York City as the place of meeting for the 1945 annual session. Certain preliminary arrangements were completed, but investigations recently made in New York clearly indicate that the necessary facilities will not be available in that city in 1945 because of conditions created by the war emergency. It is with regret that it is necessary to make the announcement that the annual session scheduled for New York, June 11 to 15, 1945, will have to be held in some other city where adequate facilities will be available. Under the direction of the Board of Trustees necessary investigations are now in progress and definite announcement as to the place of meeting for 1945 will be made through the columns of THE JOURNAL at the earliest possible time.

ANNUAL CONFERENCE OF STATE SECRETARIES AND EDITORS

The Annual Conference of Secretaries and Editors of Constituent State Medical Associations will be held at the offices of the Association in Chicago on November 17 and 18. The program will be as follows:

FRIDAY, NOVEMBER 17, 10 A. M.

Call to Order. James R. Bloss, Chairman of the Board of Trustees of the American Medical Association.

Address. Herman L. Kretschmer, President of the American Medical Association.

The Functions and Operations of the Bureau of Information. Lieut. Col. Harold C. Lueth, Army Medical Corps, Liaison Office.

The Council on Medical Service and Public Relations. John H. Fitzgibbon, Chairman of the Council.

12:30 p. m. LUNCHEON.

FRIDAY, NOVEMBER 17, 2 P. M.

Address. Roger I. Lee, President-Elect of the American Medical Association.

The EMIC Program. E. D. Plass, State University of Iowa College of Medicine, and Thurman B. Rice, State Health Officer of Indiana.

Medical Service Plans. Robert E. S. Young, Member of Medical Service Committee of Ohio State Medical Association.

FRIDAY, NOVEMBER 17, 6:30 P. M.

DINNER MEETING OF EDITORS OF STATE MEDICAL JOURNALS
PALMER HOUSE, ROOM 14, CLUB FLOOR

W. R. Brooksher, Editor of the *Journal of the Arkansas Medical Society*, presiding.

Our State Journals as Molders of Opinion. Herman M. Jahr, Editor of the *Nebraska State Medical Journal*.

Attitude of State Medical Journals Toward Political and Social Trends That May Affect Medical Affairs. Creighton Barker, Secretary of the Connecticut State Medical Society.

Our State Journals as News Services. E. M. Shanklin, Editor of the *Journal of the Indiana State Medical Association*.

SATURDAY, NOVEMBER 18, 9:30 A. M.

Medical Attitudes, Opportunities and Responsibilities in a National Fitness Program. J. W. Wilce, Ohio State University, and Member of Official Group of National Committee on Physical Fitness.

Radio Broadcasting by Medical Profession. A. S. Brunk, President of the Michigan State Medical Society.

COUNCIL ON MEDICAL SERVICE WASHINGTON OFFICE

The Washington Bureau of the Council on Medical Service is preparing a list of state association officers and the names of members designated to cooperate with it in the winter's work. The list is about complete, only a few states remaining to be heard from.

The director, Dr. Joseph S. Lawrence, has met with the county legislative chairmen of Indiana at a conference held in Indianapolis and also with the County Secretaries' Association of Wisconsin at its annual meeting.

The council has had the first of its regional meetings, held Sunday, October 29, in Cincinnati. Four states—Ohio, Indiana, Kentucky and West Virginia—composed the region and more than eighty physicians were in attendance. Dr. Edward J. McCormick, a member of the Council, presided, assisted by the three trustees, Drs. Bloss, Sensenich and Henderson, who reside in this district. The two subjects that commanded the most interest were the Council's program and the plans for prepayment insurance. The next regional conference will be held in Washington on December 6 and a third is scheduled for St. Paul on December 10.

Washington Letter

(From a Special Correspondent)

Nov. 6, 1944.

Action Promised on Capital Hospital Center Bill

Despite authorized extensions to local hospitals, efforts will be pressed immediately after the November 7 election to pass the bill to establish a 1,500 bed hospital center in the District of Columbia. Senator Millard E. Tydings (Democrat, Maryland) heads a special subcommittee of the Senate District Committee, which was created to study the measure and hold public hearings on it. He sponsored the bill in the Senate and says that every effort will be made to enact it. A companion bill was introduced in the House by Representative Thomas D'Alesandro (Democrat, Maryland) and is pending. The federal government would bear the entire cost of the proposed medical center. It would be operated on a nonprofit basis by participating private hospitals, with Emergency and Garfield Hospitals forming the nucleus.

Senator Tydings said that the cost of the center was estimated at between $5,000,000 and $7,500,000. The center would be equipped with the most modern scientific devices and staffed with the best medical personnel available. The Senate bill has been given the first position on the Senate District Committee calendar, according to Senator Theodore G. Bilbo (Democrat, Mississippi), chairman.

Robert H. Felix New Mental Hygiene Chief, Mental Hygiene Division, U. S. P. H. S.

Appointment of Dr. Robert H. Felix as medical director in charge of the Mental Hygiene Division in the Bureau of Medical Services, U. S. Public Health Service, has been announced by Dr. Thomas Parran, Surgeon General. Dr. Felix relieves Dr. Lawrence Kolb, who retired October 31. A well balanced program of the advancement of mental health in the United States was described by Dr. Felix as his first effort on taking over his new post. He cited present needs for expansion of research and a nationwide extension of psychiatric services to apply the findings of research to the psychic problems of people. Dr. Felix was borne in Downs, Ky., May 29, 1904, received his degree in medicine at the University of Colorado in 1930 and interned at the Colorado General Hospital in Denver. He was granted a two year fellowship by the Commonwealth Fund and took his postgraduate training at the Colorado Psychiatric Hospital under Dr. Franklin R. Ebaugh. He was commissioned in the regular corps of the Public Health Service in August 1933 and had a varied experience in the service. He developed and operated a mental hygiene service for the Coast Guard at New London, Conn., with the advent of war. He is a Fellow of the American Medical Association, the American College of Physicians and the American Psychiatric Association, a member of the Association of Military Surgeons and the Southern Psychiatric Association and a past president of the Kentucky Psychiatric Association.

Toxicity of DDT Described by Dr. Paul A. Neal

In spite of its inherent toxicity, DDT in the desired insecticidal concentrations in the air is of such low order that it will not cause injurious effects on human beings, said Dr. Paul A. Neal of the U. S. Public Health Service in his address to the National Museum Entomological Society here. He reported that studies conducted at the Industrial Hygiene Research Laboratory of the National Institute of Health in Bethesda, Md., showed that DDT in concentrations up to 10 per cent in inert powders for dusting clothes, as in the extermination of lice, offers no serious health consequences. The use of a 15 DDT deobase mist mixture had no toxic effect on rabbits, and it should be safe to use as a fly spray. In a clinical and laboratory study of 3 men who had had several months' continuous occupational exposure to DDT in its various forms as an insecticide, an evaluation of results failed to indicate any definite toxic effects from exposure to DDT. Although this study dealt only with the appraisal of the potential dangers of DDT when inhaled as an aerosol, dust or mist, Dr. Neal pointed out that massive doses either by mouth or by skin absorption will cause toxic reactions. Heavy contamination of foods should be avoided.

National Hospital Service Society Ordered Dissolved

Dissolution of the National Hospital Service Society, Inc., of Washington, D. C., fraternal organization providing hospitalization insurance and medical care for 5,000 District of Columbia residents, was ordered by the federal government on technical charges of violating insurance laws. District Court Justice F. Dickinson Letts consented to transfer of the five thousand policies to National Hospitalization, Inc., in Maryland. Attorneys for National Hospital Service Society state that its members do not face any loss of money or insurance benefits. Justice Letts signed a consent decree through which Cornelius H. Doherty and Louis M. Denit, attorneys, agreed to revocation of the organization's charter and dissolution of the business effective Jan. 15, 1945. U. S. Attorney Edward M. Curran and his aide Daniel B. Maher said that under terms of the charter the society was a fraternal and benefit association required to carry on its business for the sole benefit of members and beneficiaries and not for profit. The government, however, charged that the society conducted its business for profit and issued policies that did not carry death benefits and which did not require medical examinations. Such provisions were ordered for potential policyholders under the terms of the charter. The organization was founded in 1935.

Named to Joint Committee on Physical Fitness

Chairman John B. Kelly of the National Committee on Physical Fitness of the Federal Security Agency announced here that Capt. Raymond Wells, U.S.N.R., and Dr. Lon W. Morrey have been appointed to the committee as representatives of the American Dental Association. Dr. Wells is a past president of the American Dental Association, and Dr. Morrey is a member of its central office staff.

Society Proceedings

COMING MEETINGS

American Society of Anesthetists, New York, Dec. 14. Dr. McKinnie L. Phelps, 745 Fifth Ave., New York 22, Secretary.

Annual Conference of State Secretaries and Editors, Chicago, Nov. 17-18. Dr. Olin West, 535 N. Dearborn St., Chicago, Secretary.

New York State Association of Public Health Laboratories, Albany, Nov. 17. Miss Mary B. Kirkbride, New Scotland Ave., Albany 1, Secretary.

Puerto Rico, Medical Association of, Santurce, Dec. 15-17. Dr. E. Martinez-Rivera, P. O. Box 3866, Santurce, Secretary.

Southern Medical Association, St. Louis, Mo., Nov. 13-16. Mr. C. P. Loranz, Empire Building, Birmingham 3, Ala., Secretary.

Southern Surgical Association, Hot Springs, Va., Dec. 5-7. Dr. Alfred Blalock, Johns Hopkins Hospital, Baltimore 5, Secretary.

Western Surgical Association, Chicago, Dec. 1-2. Dr. Arthur R. Metz, 250 East Superior St., Chicago, Secretary.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ALABAMA

Changes in Health Personnel.—Dr. John I. Mitchell, Double Springs, health officer of Winston County for three years, has resigned effective October 1 to enter private practice either in Russellville or in Pell City, it was reported. ——Dr. Frank M. Hall, Athens, has been named health officer of Alachua County, Gainesville, Fla.

ARIZONA

State Meeting to Be in Tucson.—The Arizona State Medical Association will hold its annual meeting at the Pioneer Hotel, Tucson, April 27-28, 1945. The scientific program will be presented by members of the staff of Baylor University College of Medicine, Houston, Texas.

CALIFORNIA

Symposium on Psychotherapy.—The San Francisco Psychoanalytic Society held its semiannual meeting October 28-29 at the Ambassador Hotel, Los Angeles. One session was a symposium on short psychotherapy with Comdr. Uno H. Helgesson (MC) on "Experiences with Short Psychotherapy in Military Psychiatry"; Dr. Bernhard Berliner, San Francisco, "The Practice of Short Psychoanalytic Psychotherapy," and Drs. Otto Fenichel and Ernst Simmel, Los Angeles, "Theoretical Considerations of the Indications, Limitations and Technic of Short Psychotherapy." Other speakers include Drs. Emanuel Windholz, San Francisco, on "The Possibilities and Limitations of Group Psychotherapy" and Jacob S. Kasanin, San Francisco, "Vestigial Roots of Schizophrenia."

State Board Activities.—Superior Judge Emmet H. Wilson on September 12 upheld an order of the Board of Osteopathic Examiners revoking the license of Leslie R. Nunn, osteopath, on charges that he aided an unlicensed person in performing a tonsillectomy on 2 boys who died following an operation (THE JOURNAL, Oct. 23, 1943, p. 495). According to the Los Angeles *Examiner*, September 13, Nunn had asked for a writ of mandate compelling the board to vacate its order revoking his license as a "physician and surgeon" and charged that the board accepted evidence without his knowledge. Nunn and Harry Navarre, a chiropractor, are now in San Quentin serving terms for the deaths of 2 children who were operated on by them, it was stated.——The San Jose *Mercury Herald*, September 16, reported that probation had been granted to William G. Cardew, chiropractor and confessed abortionist. The period of the probation, which is the second in two years, is for five years. Superior Judge William F. James, in addition to making surrender of the license and abandonment of practice, equipment and drugs conditions of the probation order, also stipulated that Cardew's premises be opened for inspection at all times by county or medical authorities. Another chiropractor, Max Otto Garten, Salinas, was reported on September 17 to have been released on $2,000 bail following his arrest on a charge of performing an illegal operation.

DELAWARE

Society News.—Dr. Percy F. Pelouze, assistant professor of urology, University of Pennsylvania School of Medicine, Philadelphia, addressed the New Castle County Medical Society of Delaware, Wilmington, October 17, on "Gonorrhea and Its Treatment." Col. Arthur P. Hitchens, M. C., discussed "Public Health and the Practicing Physician" before the society on September 19.

DISTRICT OF COLUMBIA

Dr. Ruffin Honored.—Dr. Sterling Ruffin, professor emeritus of medicine, George Washington University School of Medicine, was honored when the October issue of the George Washington University news bulletin was dedicated to him. The news bulletin is entitled "Confidential—from Washington" and contains a tribute by Cloyd H. Marvin, LL.D., president of the university, in which he declares that Dr. Ruffin, "as a distinguished practitioner and able teacher of medicine, has contributed greatly to the medical school and through it to the Washington community." Dr. Ruffin graduated at the medical school in 1890, serving as professor there from 1902 to 1924, when he became emeritus.

ILLINOIS

Postgraduate Conference.—The Postgraduate Conference of Northern Illinois will be held at the Faust Hotel, Rockford, November 15. Among the speakers will be:

Mr. John W. Neal, secretary, committee on medical service and public relations, Illinois State Medical Society.
Dr. William H. Cassels, Chicago, Anesthetic Emergencies.
Dr. Robert S. Berghoff, Chicago, Heart Clinic with Demonstration of Patients.
Dr. Henry G. Poncher, Chicago, Management of Rheumatic Fever.
Lieut. Col. Okla W. Sicks, M. C., Penicillin: Its Practical Applications, with Case Reviews.
Lieut. Col. Earl R. Denny, M. C., Use and Abuse of Sulfa Drugs.

New Ruling on Boric Acid.—Dr. Roland R. Cross, Springfield, state director of public health, has requested hospitals in the state to eliminate boric acid from the inventory of drugs and other preparations kept on hand for use in the maternity divisions of the hospitals. The action was taken on the ground that boric acid is of very little, if any, antiseptic value but is highly toxic when ingested by infants. The request followed the death of 2 infants in an Illinois hospital attributed to boric acid poisoning. "The infant deaths reported from various hospitals throughout the country as due to boric acid poisoning have had their origin in the accidental substitution of boric acid powder for dried milk products or of the accidental substitution of weak boric acid solution for distilled water in the preparation of infant food formulas. Carelessness, improper labeling of bottles and shifting personnel seem to be contributory factors" Dr. Cross announced.

Chicago

Personal.—Dr. Louis J. Halpern has been appointed assistant professor of pediatrics at the University of Illinois College of Medicine.——Mrs. Adaline Hayden has been appointed executive secretary of the American Association of Medical Record Librarians, effective October 23. Her headquarters will be in the office of the American Hospital Association, 18 East Division Street.——Dr. Orpheus W. Barlow, formerly director of research laboratories of Winthrop Chemical Company, has been appointed medical and research director of Nutrition Research Laboratories. Dr. Barlow graduated at Rush Medical College in 1936.

Memorial Service for Dr. Besley.—A memorial service for the late Dr. Frederic Atwood Besley, Waukegan, will be held under the auspices of the American College of Surgeons in Memorial Hall, 50 East Erie Street, November 19, at 3 p. m. Dr. Irvin Abell, Louisville, Ky., chairman of the board of regents of the college, will preside. Taking part in the program will be Rev. Howard E. Ganster, Rector, Christ Episcopal Church, Waukegan; Dr. Irving S. Cutter, emeritus dean, Northwestern University Medical School; Major General Robert U. Patterson, M. C. (retired), Baltimore, formerly surgeon general of the Army; Dr. Gilbert J. Thomas, Los Angeles, regent, American College of Surgeons, and Dr. Donald C. Balfour, Rochester, Minn., associate, editorial staff, *Surgery, Gynecology and Obstetrics*. Dr. Besley, at the time of his death on August 16, was secretary of the American College of Surgeons, of which he was a founder-fellow in 1913.

Tumor Diagnostic Service Inaugurated.—The University of Illinois College of Medicine and the division of cancer control of the state department of public health are cooperating in a new tumor diagnostic service at the Research and Educational Hospitals, Chicago. The operation of this service under these joint auspices provides for an augmentation of the facilities offered by the tumor clinic of the medical college, which has been conducted for some time under the direct supervision of Dr. Danely P. Slaughter, assistant professor of surgery at the medical school. The activities of the state division of cancer control are under the direction of Dr. Raymond V. Brokaw, chief of the division. These facilities are available to all practicing physicians throughout the state as a consultation service in the care of their suspected cancer cases. Patients who can afford to pay will be diagnosed and returned to their referring physician with recommendations for treatment. Medically indigent patients who are approved by the social welfare department of the hospital will be treated without charge in accordance with the customary policy. Tumor clinic sessions are held on Tuesdays, Wednesdays and Fridays from 2 to 5 p. m. Ambulant patients will be admitted to the clinic on any of these days, but cases requiring hospital care will be received only by previous arrangement and to the extent of available facilities. Additional tumor diagnostic services now operated under the auspices of the division of cancer control are located at St. Anthony's Hospital, Rockford; Burnham City Hospital, Champaign, and Memorial Hospital, Springfield. At all of these services specimens of suspected tumor tissue from medically indigent patients which may be submitted by physicians from any part of the state are accepted for microscopic examination and diagnosis without charge. Suitable containers for mailing such specimens are available upon request. Further information regarding these facilities may be obtained by addressing the Division of Cancer Control, 505 South 5th Street, Champaign, or the director of any of the services named.

INDIANA

Personal.—Dr. David A. Boyd Jr., professor of psychiatry, Indiana University School of Medicine, Indianapolis, has been made the first full time director of the neuropsychiatric ward of the Indianapolis City Hospital.——Dr. Charles A. Miller, Princeton, has been appointed health officer of Gibson County, succeeding the late Dr. Bertis C. Gwaltney, Fort Branch.——Dr. Karl R. Luthy, formerly of Paducah, Ky., has been named medical director of the U. S. Rubber Company plant in Mishawaka.

LOUISIANA

Dr. Bayley Goes to Oklahoma.—Dr. Robert H. Bayley, associate professor of medicine, Louisiana State University School of Medicine, New Orleans, resigned September 1 to become professor of medicine at the University of Oklahoma School of Medicine, Oklahoma City.

MARYLAND

Evander F. Kelly Dies.—Evander F. Kelly, Phar.D., a member of the Maryland State Department of health since 1920 and secretary of the American Pharmaceutical Association, died at his home in Texas, Baltimore County, October 27. Dr. Kelly had been dean of pharmacy at the University of Maryland from 1918 to 1926, when he became advisory dean. In 1933 he won the Remington Medal of the American Pharmaceutical Association.

Emmett Holt Goes to New York Medical College.—Dr. L. Emmett Holt Jr., since 1930 associate professor of pediatrics at Johns Hopkins University School of Medicine, Baltimore, has been appointed professor of pediatrics at the New York University College of Medicine and director of the pediatric service at Bellevue Hospital. Dr. Holt graduated at Johns Hopkins in 1920 and has been a member of the staff there since 1922. He was president of the Society for Pediatric Research in 1939.

MICHIGAN

Bequest for Cancer.—About one million dollars of the estate of Mrs. James T. Pardee, Midland, is to be used for the control of cancer under her will, the New York *Times* reported October 12.

Personal.—Dr. John H. Law, formerly assistant director of Grace Hospital, Detroit, has been named director, succeeding the late Dr. Edmund F. Collins.——Dr. Milton H. Erickson, assistant professor of psychiatry at Wayne University College of Medicine, Detroit, has recently been promoted to associate professor of psychiatry.——Dr. Henry J. Pyle, Muskegon, has resigned as school physician of Muskegon, a position he has held for the past twenty-four years.

State Division of National Physicians Committee.—The Michigan Division of the National Physicians Committee for the Extension of Medical Services was organized at the Book-Cadillac Hotel, Detroit, October 11. Dr. Clarence E. Umphrey, Detroit, who has served for a number of years as chairman of the Metropolitan Detroit Group, was unanimously elected chairman of the state committee, which will now absorb the former Metropolitan organization. Other officers chosen include Drs. William M. LeFevre, Muskegon, vice chairman; Eldwin R. Witwer, Detroit, secretary, and Wyman D. Barrett, Detroit, treasurer. These officers will consider the appointment of an executive secretary.

Scholastic Prizes.—The Distinguished Service Award of Wayne University College of Medicine, Detroit, was presented during the recent commencement to Dr. Kenneth E. McIntyre as the "student outstanding in scholastic and extracurricular activities." Dr. Donald E. Preshaw received the Alumni Award, presented to the student who has maintained the highest scholastic standing during his four years in college. The Theodore A. McGraw Memorial Award, given to the outstanding student of the junior year, went to Peter J. Talso. This prize was given to Dr. Preshaw during his junior year. Arthur D. Harris and Dr. Addison E. Prince received the H. Peyton Johnson scholarships, presented annually to Negro medical students of high ability and character. The Angus McLean Memorial Award, for the graduate student who has done the best research work during the year, went to Dr. Robert O. Bauer.

NEW HAMPSHIRE

Health Program at Colby College.—Seventeen physicians conducted an annual health clinic at the Colby Junior College, for women, New London, October 21, examining the 190 entering students and reviewing the cases of returning students whose previous health records have not been perfect. Serving as the basis for the clinical work are the records presented by the student's family physician and results of the college's preliminary examination covering chest x-ray, hemoglobin test, heart rate, blood pressure, Wassermann test, urinalysis, blood analysis and audiometric reading. Following her examination, each student meets with one of the conference physicians to clear up any questions and to determine her health program for the year. Where necessary appointments are made at neighboring clinics and hospitals for psychiatric treatment and dental work. In preparation for the clinic, three medical technicians, graduates of Colby, have worked at the New London Hospital for two days to analyze specimens and to complete Wassermann tests. Undergraduates in the medical technician and medical secretarial courses receive practical experience at the clinic in making records and otherwise assisting the doctors. In addition to its purpose in preventing disease and discovering physical weaknesses, the clinic is considered an effective educational measure in that it familiarizes students with complete, efficient and modern medical methods and, through the personal doctor-student conference, gives them an opportunity to gain the maximum knowledge from the experience. The estimated expense to the college for the one day clinic is approximately $2,000. The college stresses the importance of student, faculty and staff health throughout the year. Faculty, housekeepers and groundsmen are required to pass a complete physical examination at least every three years, while food handlers must undergo an annual examination that is thorough in every respect and designed to discover carriers of infection. A daily clinic is held every morning for students to check on slight illnesses and to segregate immediately those who need hospitalization in the college infirmary.

NEW YORK

Another Medical Plan.—At a meeting October 17 the Medical Society of the County of Monroe voted to launch the Genesee Valley Medical Care Inc., a nonprofit medical insurance plan for residents of the Rochester area. The name was selected to make the plan broad enough to attract medical persons in the area but outside Monroe County. A board of ten directors and two others to be named by the president of the society, Dr. Benedict J. Duffy, Rochester, will work with six lay members of the board of directors in planning details to submit to interested agencies.

Meeting of Public Health Laboratories.—The New York State Association of Public Health Laboratories will meet at the state laboratory, Albany, November 17. Among the speakers will be:

Dr. William Kaufmann, Albany, Laboratory Aids in the Diagnosis of Amebic Colitis in Temperate Climates.
Dr. Nathan Mitchell, Albany, Latent Primary Carcinoma of the Thyroid Gland.
Dr. Frank W. Foote Jr., Albany, Mucoepidermoid Tumors of Salivary Glands.
Dr. Max M. Strumia, Bryn Mawr, Pa., Fractionation of Blood with Specific Reference to Modified Globin.

On November 16 the association will sponsor its fifth conference on tropical diseases in cooperation with the division of laboratories and research of the state department of health. Participating will be Dr. George M. Lewis, New York, who will discuss "Clinical and Immunological Aspects of Fungus Infection" and Rhoda W. Benham, Ph.D., New York, "Laboratory Procedures in the Diagnosis of Fungus Diseases."

Resources to Be Pooled in Poliomyelitis Care.—A plan is under consideration in New York State whereby personnel resources can be pooled to meet the need for postacute and convalescent care of victims of this year's outbreak of infantile paralysis. At a meeting of hospital administrators called by the state department of health, September 26, Dr. Edward S. Rogers, assistant commissioner for medical administration, stated that the estimate of cases in upstate New York will reach 4,000 by the end of the present outbreak, now past its peak, equaling the figure for the epidemic of 1916. According to *Health News*, publication of the state department of health, this does not hold true for New York City, the expected total for which is 1,800 cases, only about one fifth of the number experienced in 1916. The group attending the meeting expressed serious concern over the problem in future months of providing the facilities required to meet upstate demands and a resolution was approved providing for the appointment by the state commissioner of health of an advisory coordinating committee to consist of three representatives of each of the following groups: the Hospital Association of New York State, the New York State Association of Institutions for the Physically Handicapped and the New York State Department of Health. A function of the committee will be, among other things, to evaluate the needs of the postepidemic poliomyelitis period and to make recommendations to the commissioner of health concerning the allocation of personnel and patients to institutions qualified to care for such patients.

New York City

The Harvey Lecture.—Selman A. Waksman, Ph.D., microbiologist, Agricultural Experiment Station, State of New Jersey, New Brunswick, will deliver the second Harvey Society Lecture of the current series at the New York Academy of Medicine November 16. His subject will be "Production and Nature of Antibiotic Substances."

Industrial Hygiene Courses.—A series of one week courses in the medical, surgical and dental aspects of industrial hygiene opened at the DeLamar Institute of Public Health, Columbia University, October 30, and will continue to December 16. The program is designed to aid in the institute's expanding plan for teaching, practice and research in various aspects of public health. Studies in diagnosis and control of dermatoses began October 30. Other courses will be on general health in industry, to start November 13; the use of plasticisers and solvents in industry and their toxicologic aspects, November 20; metals and their industrial uses and dangers, November 27, and the administrative aspects of industrial hygiene, December 4. Dental problems and practices in the field of industrial hygiene will be the subject of the final course in the series, to begin on December 11.

Rehabilitation Project.—The Hospital for Joint Diseases and the New York City Vocational Rehabilitation Bureau have worked out a joint program directed toward the early vocational rehabilitation of patients known to that hospital. The plan calls for an analysis of the social and vocational needs of the patients based on the medical survey; diagnosis and prognosis before patients are discharged from the hospital. Consideration will be given as to whether a patient can return to his former job, whether he requires assistance in returning to his previous job or work environment, whether he requires counseling and guidance in his job adjustment or whether he requires training or retraining toward a job objective. Where patients are discharged from the hospital to continue under medical care, consideration of medical, social and vocational needs of the patient will continue after his discharge from the hospital until the plan for the patient is fulfilled. This early consideration will aim to balance the patient's physical and psychologic capacity to the demands of the training and retraining program and the job objective as outlined. The project is under the direct guidance of the medical board, which has assigned several of its members to the rehabilitation committee. In this project, in which the doctors will take leadership, all departments of the hospital will be involved, including medical, nursing, social service, occupational therapy and physical therapy. The New York City Vocational Rehabilitation Bureau has assigned a member of its staff to the joint rehabilitation project who is serving at the hospital.

Postwar Plans Feature Dinner for Physicians.—A dinner was held at the Hotel Roosevelt, October 26, celebrating the seventieth birthday of Drs. Samuel A. Brown, formerly dean of the New York University College of Medicine, and George B. Wallace, professor of pharmacology at the college. The occasion also observed the many years of service of both physicians, Dr. Brown having been associated with the college since 1896, two years after his graduation there, and Dr. Wallace, who has been associated with the teaching faculty since 1901. Dr. Brown served as dean from 1915 to 1932. He is currently chairman of its council committee on medicine and dentistry. Harry Woodburn Chase, LL.D., chancellor of the university, as a guest speaker, announced extensive postwar plans for the development of a medical-dental center in the Bellevue area by the New York University College of Medicine in cooperation with the city of New York and Bellevue Hospital. The plans would include a university hospital and diagnostic clinic which would offer all methods of modern diagnosis together with inpatient facilities to families of the middle-low income group; an institute of medical sciences where the clinical departments of medicine can offer opportunities to younger men for study and research in specially important fields and a general unit which would comprise the medical library, hall of residence and a large auditorium for postgraduate teaching to seat 500. In announcing the proposed plans, Dr. Chase paid tribute to Dr. Brown and Dr. Wallace for their efforts in the development of the New York University College of Medicine.

OREGON

Frank Menne Retires as Professor of Pathology.—Dr. Frank R. Menne, since 1916 associated with the University of Oregon Medical School, Portland, has resigned as professor and head of the department of pathology. He has been succeeded by Dr. Warren C. Hunter, a member of the staff of the school since 1925. Dr. Menne graduated at Rush Medical College in 1915, going to Oregon the following year to become assistant professor of pathology. He was named professor in 1920 and head of the department in 1929. Dr. Hunter graduated at Oregon in 1924, joining the faculty the following year as assistant professor of pathology. He was named professor in 1941.

RHODE ISLAND

Fraudulent License Revoked.—On August 9 the state board of medical examiners revoked the license to practice medicine issued to Charles Jacobson, 984 Broad Street, Providence. Appeal by Jacobson subsequent to this action serves as a stay of the revocation until the case is disposed of by the supreme court. The state board of medical examiners contends that Jacobson obtained his license to practice through fraud and deceit. It is reported that there is no evidence to prove that Jacobson had taken and passed his state examination in 1934 as he claimed, and members of the board testified that they did not recall that he took the examination. A physician testifying at the trial, who took the examination in question, testified that he did not see Jacobson present at the time and that Jacobson later came to him and asked him to state that he had seen the latter take the examination. Information concerning Jacobson shows that he graduated at the Middlesex College of Medicine and Surgery, Waltham, Mass., in 1932 and served an internship at the Miriam Hospital, Providence, from July 1932 to July 1933. He is reported to have taken the Massachusetts State Board examinations in 1934 and 1935, failing to pass in either of them.

SOUTH CAROLINA

Changes in Health Officers.—Dr. Robert D. Hicks, director of the York and Chester district health department, has also been placed in charge of the unit at Cherokee County with headquarters in Chester.—Dr. James N. Holtzclaw, director of the Greenville County Health Department, has been given jurisdiction over the unit in Laurens County.

Young Physician Wins Ravenel Cup.—Lieut. (jg) Harry Boatwright (MC), who graduated at the Medical College of the State of South Carolina, Charleston, September 16 and who has received a commission in the U. S. Naval Reserve, was during his graduation exercises presented with the Ravenel Cup for his thesis in the field of public health. The cup is awarded annually by Dr. Mazyck P. Ravenel, formerly of Charleston and now emeritus professor of medical bacteriology and preventive medicine in the University of Missouri School of Medicine, Columbia.

TEXAS

Proposed Expansion Program at State Medical School.—Chauncey D. Leake, Ph.D., dean and executive vice president, University of Texas School of Medicine, Galveston, recently recommended a long range expansion program estimated to cost about four million dollars to meet the physical needs of the school of medicine. The recommendations were contained in a report to the medical committee of the board of regents of the university and include an addition of the main laboratory building to cost $1,000,000, a library auditorium and general administration building $300,000, and a building for a school of public health which, according to the state medical journal, probably could be housed in the main building of the medical college if other departments are transferred. The transfer of the Galveston State Psychopathic Hospital to the medical college to provide exceptional facilities for psychiatry was also recommended. Immediate needs proposed by Dr. Leake include: estimated repair costs, $10,000; pediatric clinical laboratories, $2,500, which will come from the Buchanan Foundation; pediatric experimental facilities, $15,000 from the Buchanan fund; housing for women medical students, $40,000, and locker rooms for hospital help, $12,000. Dr. Leake also recommends that legislative appropriations be increased to provide appropriate salaries to insure additional teachers necessary to reach a reasonable approach of the optimum teacher-student ratio for American medical schools of one instructor to ten students per course, and that a salary scale be provided that will assure competent teachers and research workers. The salary range in the preclinical departments of the better medical schools of the United States, it was stated, is as follows: for full time faculty members—professor, $12,000 to $16,000; associate professor, $6,000 to $10,000; assistant professor, $4,500 to $8,000; instructor, $3,000 to $6,000; assistant, $2,000 to $3,600.

WEST VIRGINIA

Questionnaires to Determine Psychiatric Program.—Results of questionnaires will be presented to the council of the West Virginia State Medical Association at its meeting this month to determine what part, if any, the association will take to provide a general program on psychiatric education for practicing physicians in the state. Of the 350 physicians whose questionnaires have been reviewed, 90 per cent would like additional knowledge on psychiatry and at least 80 per cent would like to know more about emotional illness. Less than 15 per cent of the physicians replying to the questionnaire sent out by the state society in August stated that they have had any training or developed any working concept in psychiatry. Almost all of the replies indicate a general lack of psychiatric assistance in the state. More than 90 per cent of the physicians are interested in seminars on psychiatry to be held evenings at meetings of component medical societies, and 50 per cent of the group expressed their willingness to pay a nominal attendance fee. Seventy per cent signified their willingness to have a symposium on psychiatry presented in the *West Virginia Medical Journal*. The returned questionnaires indicated that doctors would be willing to have psychiatry presented in simple terminology and related to general medicine, with stress being placed on the handling of psychoneuroses, subclinical personality problems and psychosomatic disturbances.

Medical Societies Merge.—On October 20 the Lewis County Medical Society was merged with the Central West Virginia Medical Society, carrying out a unanimous vote of both groups. The consolidation of the two societies will mean an active roll of more than fifty doctors. The Lewis County Medical Society includes physicians in Gilmer County, and members of the enlarged Central West Virginia Medical Society residing in six adjoining counties can conveniently meet at the county seat in any of these communities. The Lewis-Upshur Medical Society was organized in 1899 principally through the efforts of Dr. Thomas M. Hood, Clarksburg, who recently died in that city at the age of 91 years. That same year the state medical association held its annual convention at Weston and the late Dr. Charles S. Hoffman, Keyser, was elected president. In 1915 the doctors of Upshur County withdrew from the Lewis County Medical Society and became members of the Central West Virginia Medical Society, then composed of doctors residing in Nicholas, Braxton and Webster counties. Three members of the Lewis County Medical Society who were charter members at the time of the organization of the Lewis-Upshur Society are still in practice at Western and are members of the Lewis County Medical Society. These members, Drs. George Snyder, Wessie P. King and Edward T. W. Hall, are now honorary life members of the local society and the state medical association.

GENERAL

Pediatric Society Opposes Children's Bureau Transfer to Public Health Service.—At a meeting of the American Pediatric Society in Atlantic City, N. J., September 25-27, a resolution was adopted affirming the society's wish to continue the hitherto good relations between it and the Children's Bureau. Other resolutions affirmed that no change in the method of payment in the EMIC program is warranted or desirable and that the transfer of the health services of the Children's Bureau to the U. S. Public Health Service, contained in the Miller bill now before Congress, is undesirable. The resolution points out that this transfer would separate medical care from the other essential aspects of child care and emphasizes that the Miller bill does not make any provision for the development of a National Department of Health. Dr. C. Anderson Aldrich, Rochester, Minn., was chosen president of the American Pediatric Society during this meeting, Dr. Charles Hendee Smith, New York, vice president and Dr. Hugh McCulloch, St. Louis, secretary-treasurer. Dr. Heyworth N. Sanford, Chicago, is the recorder-editor.

The Poliomyelitis Situation.—The 1944 epidemic of infantile paralysis has officially become the second worst in the recorded history of the disease in the United States, the National Foundation for Infantile Paralysis announced October 29. In the first forty-one weeks of 1944, or up until October 14, there were 16,133 cases of poliomyelitis, according

to the latest report from the U. S. Public Health Service. This is 353 cases more than were reported in the country for 1931, which previously had been the second worst year for the disease. The all time record was in 1916, when there were 27,621 cases. Although the peak of the outbreak had been passed a month before this report, the epidemic itself has not yet ended, it was stated. There were 710 new cases reported for the week of October 7-14, or nearly half the weekly total at the peak of the epidemic, the week ended September 2, when 1,683 cases were reported. The seven states most severely menaced were New York, North Carolina, Pennsylvania, New Jersey, Virginia, Ohio and Kentucky, but emergency aid in the form of money, professional personnel and supplies has been sent this year by the National Foundation to twenty-one states and the District of Columbia.

Earl Bonnett Named Medical Director of Metropolitan Life.—Dr. Earl C. Bonnett, associate medical director of the Metropolitan Life Insurance Company, New York, has been appointed medical director of the company, to succeed the late Dr. Charles L. Christiernin, who died October 18. In his new capacity Dr. Bonnett will supervise a staff of about 8,000 physicians who serve as medical examiners for the Metropolitan in the United States and Canada. He will be responsible for the formulation of rules for the medical examination of applicants for insurance and advise in the establishment of rules for the selection of risks. His duties will also involve the management of home office health activities, which include the medical care and periodic physical and dental examinations of some 14,000 employees. Dr. Bonnett graduated at Cornell University Medical College in 1923 and joined the staff of the Metropolitan as a medical examiner in the home office in 1926. He was advanced to official rank as assistant medical director in 1928 and promoted to associate medical director in 1944.

Music in Therapy.—The National Music Council recently conducted a survey to ascertain to what extent music is currently used in leading nervous and mental disease hospitals throughout the country. Two hundred and nine hospitals with various bed capacities answered a questionnaire. Only 192 of the 209 used music. The rest were refrained from adopting this form of therapy by war restrictions and economics, shortage of personnel and lack of facilities. There are performances in 160 hospitals by visiting artists, gifted patients, church choirs, bands and glee clubs. Recorded music is played by 152 institutions. Only 23 hospitals reported that they used music for therapeutic reasons, and 134 used it for both recreation and therapy. According to a report in the New York *Times*, most directors of hospitals find that "recreation is therapy." Active participation in the making of music is generally considered more effective than mere listening. Group performance develops a spirit of cooperation and fellowship and helps patients to overcome their inhibitions. The psychiatric staff of one hospital finds that the blare and dissonance of jazz "is a disturbing influence to all types of patients." Band music, spirituals, American folk songs are soothing. But music is not a specific for mental disorders, it was stated; there is even the danger that the wrong music may be used by patients to express and reinforce delusional ideas.

National Research Council Named for Pharmaceutical Award.—The American Pharmaceutical Manufacturers' Association announces that the National Research Council has been chosen for its sixth annual award "in recognition of its fundamental contributions to public health in the field of medical sciences and of its essential services to the country in World Wars I and II." The award will be presented during the final day's session of the two day meeting of the American Pharmaceutical Manufacturers' Association at the Waldorf-Astoria, New York, December 11-12. Among the speakers in a program devoted to some fundamental trends in chemotherapy will be:

Dr. John S. Lundy, Rochester, Minn., Progress in Conquest of Pain by New Anesthetics.
Dr. Chester S. Keefer, Boston, Progress in Conquest of Bacteria by New Medicinal Agents.
William C. Rose, Ph.D., Urbana, Ill., Progress in Conquest of Malnutrition by Amino Acids.
Edwin J. Cohn, Ph.D., Cambridge, Mass., Progress in Conquest of Disease by Blood Proteins.
Wendell M. Stanley, Sc.D., Princeton, N. J., Progress in Conquest of Disease by Virus Proteins.

Dr. Alan Gregg, New York, director of medical sciences, Rockefeller Foundation, will give the presentation address, on "Essential Need of Fundamental Research in Medical Sciences for Social Progress," and Dr. Ross G. Harrison, New Haven, Conn., chairman of the National Research Council, the acceptance address, entitled "National Research Council and Its Action in Field of Medical Sciences."

LATIN AMERICA

Health Activities in Latin America.—*Personal.*—Lieut. Col. Leon H. Collins Jr., M. C., who practiced in Philadelphia before entering military service in 1942, has been appointed section chief at Gorgas Hospital, Ancon, Canal Zone.

Report of Health and Sanitation Division.—A summary of activities of the health and sanitation division, Office of the Coordinator of Inter-American Affairs, has recently been published. Between February 1942 and July 1943 agreements for cooperative health work were signed with fifteen of the other American republics, according to the Newsletter of the division. Mexico was added in July 1943, the Dominican Republic in August 1943 and Uruguay in November 1943. Twelve republics which arranged to extend the program for periods of two and one-half to five years include Brazil, Colombia, Costa Rica, the Dominican Republic, El Salvador, Honduras, Mexico, Nicaragua, Peru, Paraguay and Venezuela. Renegotiations for Bolivia and Guatemala are pending. The report states that more than six hundred activities are under way or completed in the southern countries including 300 jobs for environmental improvement by permanent mosquito control measures, water supplies, sewerage systems and general sanitation. Construction work includes provision or improvement of facilities for a total of about one hundred and forty health centers, hospitals, infirmaries, dispensaries and other buildings. Over two hundred activities are devoted to provision of medical care and preventive services through operation of hospitals, health centers, clinics and laboratories, surveys and research in disease control, local training courses and widespread health education for the lay public. Although the division was established in February 1942, the report indicates the expansion of its activities during the period July 1, 1943 through June 30, 1944, in which projects reported completed total one hundred and forty-three and include complete construction, additions to or remodeling of sixteen hospitals, seventeen health centers, twelve dispensaries and fifteen other buildings. Health centers were completed at Encarnacion and Concepcion and in the Barrio Obrero District of Asuncion. In the latter a combination 50 bed hospital and health center was constructed, with x-ray and laboratory sections to serve both units. Since September 1943, operation and maintenance of the hospital section has been carried on by the ministry of health, with supervision of all nursing personnel by a United States nurse serving with the field party. Operation of the health center is a cooperative project, with a Paraguayan doctor serving as health officer. Cooperative direction of medical facilities and specific disease control services was terminated by the completion of some thirty projects, many of which were turned over to the national departments of health for continuing operation. These included plague control in Ecuador and treatment services in many areas of Colombia. In other instances the closed projects consisted of prevalence surveys or were of an emergency nature, such as those in El Salvador. Here medical services were provided for the care and improvement of the health of employees on the Pan American Highway from March 10 through September 30, 1943. A medical supervisor had headquarters at Santa Rosa. Malaria surveys were made by means of routine blood smears and cases treated with quinine and atabrine. Inspections were also made periodically to diagnose and treat venereal disease. The project was in cooperation with the department of public works of the republic of El Salvador and the U. S. Army engineers in charge of the Pan American Highway. Under the professional training program arrangements were made for 212 persons from the other Americas for study or travel grants in the United States. These consisted for the most part of physicians or engineers who were enrolled in schools of public health for courses leading to certificates or degrees in this field.

CORRECTIONS

Globin Insulin.—The second article of the July issue of the *Annals of the District of Columbia* listed in THE JOURNAL, October 7, should read "Comparative Study of Action of Globin Insulin with Other Forms of Insulin. M. Protas." The word Globulin is a misprint in THE JOURNAL.

Modified Miller-Abbott Tube.—At the request of Dr. Franklin I. Harris, who wrote "A New Rapid Method of Intubation with the Miller-Abbott Tube" (THE JOURNAL, July 15) credit should be given to Dr. Ivar Sivertsen for independent use of metallic mercury in the balloon of the Miller-Abbott tube. This modification of the Miller-Abbott tube was mentioned in a paragraph in the book by Wangensteen entitled "Intestinal Obstruction," second edition, page 164.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Oct. 11, 1944.

Workmen's Compensation to Be Taken Over by the Government

The expansion of medical socialism, in the form of compulsory social insurance, has been described in a previous letter. In a further paper the government has outlined proposals for a new industrial injury insurance scheme to replace the present system of workmen's compensation. The legal liability of the employer to compensate an employee for loss of earning capacity due to accident or industrial disease arising out of his employment is swept away, and provision for disablement or loss of life from industrial injury or specified industrial diseases becomes a social service. This fundamental change is based on the recommendations of the Beveridge scheme, but the benefits are substantially more generous. Instead of being related to loss of earning capacity, as under the existing compensation law, the benefits will be paid on flat rates, with supplements for family responsibilities. A financial responsibility which rests on the employer will now be shared by him, the employee and the state. Contributions will be 12 cents a week for adult men and 8 cents for adult women, and half these rates for boys and girls under 18. Employers will pay the same amounts. The scheme will apply to the 18,000,000 employed persons in the social insurance scheme.

A workman incapacitated by an industrial injury will receive $7 a week up to thirteen weeks, with $1.75 added for a wife and $1 for the first child. Allowances for other children will also be payable under the family allowances scheme. If the disablement is likely to be permanent or prolonged, the allowance will be replaced by an industrial pension based on a medical assessment of the degree of disability. The pension rate for total disability will be $8 a week, with allowances of $2 a week for a wife and $1.50 for the first child. Benefits are also payable to a widow or to other dependents on the death of an insured person. Before the war, workmen's compensation cost employers $40,000,000 a year, which was increased to $68,000,000 by wartime legislation. Under the new scheme benefits are estimated to cost $80,000,000 annually, with a further $12,000,000 required for administration. One sixth of the cost will be borne by the state, and the rest in equal shares by employers and employees. Thus the cost to either of the latter will be something less than $40,000,000 a year. A great merit claimed for the new scheme is that it will remove workmen's compensation from the atmosphere of conflict with which it has been surrounded and avoid the ultimate recourse to litigation between employer and workman.

Sir Humphry Davy Rolleston

The death at the age of 82 of Sir Humphry Davy Rolleston, September 24, removes a prominent figure in British medicine. He came of a family distinguished in science, his father being George Rolleston, M.D., F.R.S., Linacre professor of physiology at Oxford, and his mother a niece of the physicist Sir Humphry Davy. He was educated at Cambridge, where he had a distinguished career, and at St. Bartholomew's Hospital. After serving as house physician and demonstrator of anatomy he wrote "A Manual of Practical Morbid Anatomy." He was appointed assistant physician to St. George's Hospital, where he taught pathology. He became associated with Sir Clifford Allbutt, regius professor of medicine at Cambridge, and assisted him in the preparation of his "System of Medicine" in eight volumes, which appeared from 1896 to 1899 and for many years was a leading textbook of medicine. In the revised edition, which appeared from 1906 to 1911, his name appeared as co-author. He wrote several of the articles, notably those on alcoholism, diseases of the esophagus, small intestine, adrenal glands, spleen and lymphatics. In 1925, on the death of Allbutt, he succeeded to the professorship. He was examiner in medicine in most of the universities and in 1922 was president of the Royal College of Physicians.

What distinguished him most was prodigious learning and utmost accuracy as a writer and editor. In his Harveian Oration on Cardiovascular Diseases he quoted some three hundred authors. The first important work to appear under his name was "Diseases of the Liver, Gallbladder and Bile Ducts," published in Philadelphia in 1905. A third edition, in which Prof. J. W. McNee cooperated, appeared in 1929. Among shorter works from his pen were "The Medical Aspects of Old Age," an essay on "Writing Theses for the M.B. and M.D.," which was a useful medicoliterary help, and the Osler memorial oration. He was the author of innumerable addresses and articles. In 1936 he began the editorship in twelve volumes of the British Encyclopedia of Medical Practice, writing many of the sections himself. From 1928 almost until the time of his death he was editor of the *Practitioner*. He took part in much administrative work, sitting on numerous government committees—the Medical Consultative Board for the Navy, the Medical Administrative Committee of the Royal Air Force, the Royal Commission on National Health Insurance, the Royal Commission on Lunacy and Mental Disorder and the Colonial Committee on Medical Services. In his full life he was much respected for his integrity, perfect courtesy and devotion to truth.

The Medical Staff at Arnhem

Of the 6,500 air borne troops landed at Arnhem, only 2,000 returned unwounded after nine days' almost sleepless fighting. Some 1,200 wounded had to be left behind, but a wounded officer who afterward escaped said that the Germans were treating them with consideration. The divisional medical staff of all ranks chose to stand by their patients and went with them into captivity. A staff officer stated that the action of this fine division contributed much to the success of the operation, which should be looked on not as a brilliant failure but as an expensive success.

Marriages

DOROTHY E. DONLEY, Columbus, Ohio, to Mr. Thomas P. Dowd of Somerset, Md., in Washington, D. C., September 4.

GEORGE HENRY BUNCH JR., Columbia, S. C., to Mrs. Nancy Riddleberger Hutchinson in Washington, D. C., October 1.

JOSEPH F. CORSARO, Cleveland Heights, Ohio, to Miss Dorothy Elizabeth Yopko of Munhall, Pa., September 23.

RICHARD HENRY STANTON, Newton, Mass., to Miss Elizabeth Cecelia Eichorn of West Medford, September 4.

JAMES NATHAN SLEDGE JR., Greensboro, Ala., to Miss Evelyn Camille Wohlers of Yakima, Wash., September 2.

MARVIN S. ALTER, Salt Lake City, to Miss Ellen Scott of San Gabriel, Calif., in Los Angeles recently.

WALTER RANDOLPH CHITWOOD, Wytheville, Va., to Miss Ruth Anne Reed of Willis, September 18.

THOMAS D. DUANE, Peoria, Ill., to DR. JULIA A. MCELHINNEY of Iowa City, Iowa, March 22.

THOMAS B. DANIEL, Oxford, N. C., to Miss Bette Mazgelis of Worcester, Mass., September 13.

HUGH HYDEN GREGORY, Dalton, Ga., to Miss Myrtle Louvenia Durham of Atlanta, September 21.

JAMES J. BARROCK, Milwaukee, to Miss Marie Theresa Ramy of Mankato, Minn., September 4.

LEONARD M. VAN STONE to Mrs. Emelie Culbertson Kistler, both of Denver, August 8.

SAUL ROY KOREY to Miss Doris Evelyn Broder, both of New York, October 15.

Deaths

Milbank Johnson, Pasadena, Calif.; Northwestern University Medical School, Chicago, 1893; member of the California Medical Association and the Southern California Medical Association; chairman of the special medical research committee at the University of Southern California, Los Angeles; professor of physiology and clinical medicine from 1897 to 1901; for twelve years, from 1901 to 1913, chief surgeon for the Southern California Edison Company; president of the Municipal Charities Commission, Los Angeles, from 1913 to 1917; vice president and director of the Pacific Mutual Life Insurance Company from 1917 to 1936; director of the American Insurance Federation since 1917; president of the Western States Taxpayers Conference and the California Taxation Improvement Association, 1925-1926; since 1926 chairman of the board of directors of the California Taxpayers Association; director and member of the executive committee of the National Tax Association; member of the board of directors of the Pasadena Hospital Association; served as a member of the board of health of Los Angeles from 1900 to 1904 and as a member of the board of freeholders which revised the Los Angeles city charter in 1916; member of the executive committee of the California Military Welfare Commission during World War I; member and past president of the California Conference of Social Agencies; vice chairman of the California Educational Aid Foundation; president of the Southwest Museum from 1920 to 1926; received the LL.D. from the University of Southern California in 1917 and Northwestern University in 1920; since 1942 member of the city defense council and the Red Cross Emergency; died in the Huntington Memorial Hospital October 3, aged 72.

Sidney Morrill McCurdy ✦ St. Johnsbury East, Vt.; Western Reserve University Medical Department, Cleveland, 1904; resigned in 1941 as chief medical director of the Ohio State Industrial Commission, a position he had held since 1936; during World War I served as a captain in the medical corps, 18th Infantry, first division, and had been awarded the Croix de Guerre, the Bronze Star and the Presidential citation for bravery; recommended for the Distinguished Service Medal; member of a committee on industrial sanitation formed in 1915 by the Section on Preventive Medicine and Public Health of the American Medical Association; lecturer on industrial medicine at the Ohio State University College of Medicine, Columbus for many years; past president of the Mahoning County (Ohio) Medical Society; formerly chief surgeon of the Youngstown Sheet and Tube Company in Youngstown, Ohio, and medical director of the Plumbrook Ordnance Works in Huron, Ohio; served as a member of the staffs of the Youngstown Hospital, Youngstown, Ohio, and the Brightbrook Hospital, St. Johnsbury; died September 26, aged 63.

Ralph Garfield Mills ✦ Decatur, Ill.; Northwestern University Medical School, Chicago, 1907; an Associate Fellow of the American Medical Association; aided in building the Kennedy Hospital, Kangkai, Korea, of which he was head from 1908 to 1912; professor of pathology and bacteriology and in charge of the clinical laboratories and research department, Severance Union Medical College, Seoul, Korea, from 1913 to 1918; served as head of the department of pathology in Peking Union Medical College and as instructor in pathology at Johns Hopkins University, Baltimore; formerly professor and head of the department of pathology at the University of Colorado School of Medicine, Denver; entered the Mayo Clinic, Rochester, Minn., as an associate in pathologic anatomy and later became professor of pathology at the University of Minnesota Graduate School; formerly on the staff of St. Agnes Hospital, Fond du Lac, Wis.; member of the American Association of Pathologists and Bacteriologists and the Wisconsin Academy of Science; died in St. Mary's Hospital October 17, aged 63.

Laird Sumner Van Dyck ✦ New York; Rush Medical College, Chicago, 1924; associate in dermatology and syphilology at the New York Post-Graduate Medical School, Columbia University; specialist certified by the American Board of Dermatology and Syphilology; member of the American Academy of Dermatology and Syphilology; diplomate of the National Board of Medical Examiners; served on the staffs of the Welfare Hospital for Chronic Diseases and the New York Skin and Cancer Hospital; chief of clinic, attending dermatologist and syphilologist to the dispensary, and assistant attending dermatologist and syphilologist, New York Post-Graduate Hospital, where he died August 9, aged 51, of generalized lymphosarcomatosis.

Edward Charles Podvin ✦ New York; Albany Medical College, Albany, N. Y., 1898; member of the House of Delegates of the American Medical Association in 1941, 1942 and 1943; assistant secretary of the Medical Society of the State of New York; executive secretary and past president of the Bronx County Medical Society; past president of the Catholic Physicians' Guild; chairman of the Bronx Tuberculosis and Health Committee; on the consulting staffs of the Fordham and St. Francis hospitals; in 1935 appointed by Governor Lehman a member of the state industrial council; editor of the *Bulletin of the Bronx County Medical Society;* died September 27, aged 68, of arteriosclerosis.

James Moorhead Murdoch ✦ Pittsburgh; Western Pennsylvania Medical College, Pittsburgh, 1892; member of the American Psychiatric Association, the Central Neuropsychiatric Association and the Association for Research in Nervous and Mental Disease; president of the American Association on Mental Deficiency in 1903 and secretary from 1917 to 1921; formerly instructor in histology and pathology at his alma mater; for many years physician and superintendent of the State Institution for the Feebleminded of Western Pennsylvania, Polk; superintendent of the Minnesota School for Feebleminded at Faribault from 1927 to 1937, when he resigned; died October 9, aged 75.

Saul Berman ✦ Boston; Harvard Medical School, Boston, 1920; specialist certified by the American Board of Obstetrics and Gynecology, Inc.; formerly assistant in obstetrics at his alma mater; served an internship at the Boston City Hospital; formerly a resident physician at the Boston Lying-in Hospital; on the staffs of the Newton Hospital, Newton, Massachusetts Women's Hospital, New England Hospital for Women and Children and the Boston Lying-in Hospital; founder of the fertility clinic and laboratory at the Beth Israel Hospital; died in the New England Deaconess Hospital September 18, aged 48, of carcinoma of the testis and uremia.

Harlan Herbert Staats ✦ Charleston, W. Va.; Barnes Medical College, St. Louis, 1899; an Affiliate Fellow of the American Medical Association; honorary member of the Kanawha County Medical Society and the West Virginia State Medical Association; during World War I served in the medical corps of the U. S. Army as a plastic surgeon with evacuation hospital number 41 and had been honorably discharged with the rank of captain; founder and president of the Staats Hospital; formerly surgeon in charge of the Roane County Hospital, Spencer; died in a Huntington hospital September 30, aged 68, of myocardial failure.

Wilbur Stuart Wood, Decatur, Ill.; University of Illinois College of Medicine, Chicago, 1925; member of the American Academy of Orthopaedic Surgeons and the Illinois State Medical Society; specialist certified by the American Board of Orthopaedic Surgery, Inc.; served with the 149th Field Artillery in France during World War I; formerly an intern at St. Luke's Hospital in Chicago; past president of the Macon County Tuberculosis and Visiting Nurses' Association; on the staffs of the Decatur and Macon County and St. Mary's hospitals; died in Minoqua, Wis., August 7, aged 44, of coronary thrombosis.

Henry Carter Metcalf ✦ Connersville, Ind.; University of Louisville Medical Department, Louisville, Ky., 1913; served as a member and at the time of his death president of the Indiana State Board of Health; served as secretary of the Fayette County Board of Health, county coroner and president of the Fayette-Franklin Counties Medical Society; served overseas as a first lieutenant with the 163d Depot Brigade, 132d Engineers during World War I; member of the Connersville Board of Health; director of the Central State Bank; died in the Fayette Memorial Hospital, September 23, aged 56, of hypertensive vascular disease.

William Edwin Joiner, Seattle; Bellevue Hospital Medical College, New York, 1898; member of the Washington State Medical Association and the Pacific Coast Oto-Ophthalmological Society; served during World War I; lieutenant colonel, medical reserve corps, U. S. Army, not on active duty; for many years affiliated with the Veterans Administration; at one time served as assistant eye surgeon at the Brooklyn Eye and Ear Hospital, Brooklyn; died in the Veterans Administration Facility, Portland, Ore., August 7, aged 74, of bronchogenic carcinoma.

John Robert Abercrombie ✦ Baltimore; University of Maryland School of Medicine, Baltimore, 1895; formerly associate professor of dermatology at his alma mater; served as professor of materia medica and dermatology at the Woman's Medical College of Baltimore; died August 3, aged 75.

George Sheldon Adams ✠ Yankton, S. D.; Rush Medical College, Chicago, 1901; member of the American Psychiatric Association; medical superintendent of the Yankton State Hospital; on the staff of the Sacred Heart Hospital, where he died July 28, aged 67, of chronic endocarditis and acute dilatation of the heart.

James Tevis Arwine, Santa Rosa, Calif.; University of the South Medical Department, Sewanee, Tenn., 1894; member of the American Psychiatric Association; served during World War I; served on the staffs of various Veterans Administration facilities, including the one at Palo Alto, where he died August 24, aged 71, of arteriosclerotic heart disease.

Albra W. Baker, Elizabethtown, Pa.; State University of Iowa College of Homeopathic Medicine, Iowa City, 1887; died in the Masonic Home August 16, aged 85, of cerebral hemorrhage and arteriosclerosis.

William A. D. Barnhill, Laotto, Ind.; Cleveland Medical College, Homeopathic, 1893; died in the Methodist Hospital, Fort Wayne, September 25, aged 84, of pneumonia following a fracture of the left femur received in a fall.

Stephen Vincent Bedford, Jefferson City, Mo.; University of Missouri School of Medicine, Columbia, 1903; member of the Missouri State Medical Association; served as president of the Cole County Medical Society; on the staff of St. Mary's Hospital; chief surgeon for the Missouri Pacific Railroad; died August 23, aged 63, of myocarditis and multiple neuritis.

Edison William Brown, Revere, Mass.; Tufts College Medical School, Boston, 1905; member of the Massachusetts Medical Society; on the staffs of the Winthrop Community Hospital, Winthrop, Whidden Memorial Hospital, Everett, and the Chelsea Memorial Hospital, Chelsea, where he died August 18, aged 67, of coronary thrombosis.

William King Campbell ✠ Long Branch, N. J.; University of Pennsylvania Department of Medicine, Philadelphia, 1900; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; past president of the Monmouth County Medical Society; chief of the eye, ear, nose and throat department, Monmouth Memorial Hospital; vice president of the Long Branch Building and Loan Association; died September 21, aged 65, of coronary thrombosis.

Charles Leonard Christiernin ✠ Maplewood, N. J.; Harvard Medical School, Boston, 1906; member of the Massachusetts Medical Society; in 1916 became assistant medical director and in 1935 medical director of the Metropolitan Life Insurance Company, New York; a member of the executive committee of the Association of Life Insurance Medical Directors, of which he had been treasurer, vice president and president; died suddenly October 18, aged 66, while on a vacation in Coreys, N. Y., of coronary thrombosis.

Francis Xavier Crawford, Boston; Harvard Medical School, Boston, 1898; member of the Massachusetts Medical Society; on the staffs of St. Elizabeth's and Carney hospitals; medical director for the United Fruit Company; died August 19, aged 71, of cerebral hemorrhage.

LIEUT. WILLIAM C. CRAIG, M. C., A. U. S., 1910-1944

LIEUT. TENNYSON G. JOHNSON M. C., A. U. S., 1915-1944

MAJOR BERTRAM W. MORSE M. C., A. U. S., 1901-1944

Emilio Deantonio ✠ Scranton, Pa.; Regia Università degli Studi di Pavia Facoltà di Medicina e Chirurgia, Italy, 1894; in June 1944, presented with a testimonial plaque by the Medical Society of the State of Pennsylvania in recognition of fifty years of practice; formerly associated with the Scranton Private Hospital; died August 28, aged 72.

Bernard Walker Donohue, Baltimore; University of Maryland School of Medicine, College of Physicians and Surgeons, Baltimore, 1931; served an internship at the University of Maryland Hospital and the Bon Secours Hospital; served a

KILLED IN ACTION

William C. Craig, Waynesboro, Pa.; Ohio State University College of Medicine, Columbus, 1935; member of the Medical Society of the State of Pennsylvania; served an internship at the Allegheny General Hospital, Pittsburgh; commissioned a first lieutenant in the medical corps, Army of the United States, Sept. 4, 1942 and began active duty Oct. 15, 1942; a flight surgeon in the air corps; killed in action in the South Pacific area April 28, aged 33.

Tennyson Gates Johnson, Kerkhoven, Minn.; University of Minnesota Medical School, Minneapolis, 1943; served an internship at the City of Detroit Receiving Hospital, Detroit; commissioned a first lieutenant in the medical corps, Army of the United States, on Aug. 6, 1942; began active duty on July 3, 1943; killed in action in the European area July 13, aged 28.

Bertram Wallace Morse, Whitehall, Mich.; Detroit College of Medicine and Surgery, 1932; member of the Michigan State Medical Society; served an internship at the Henry Ford Hospital in Detroit; served as health officer and as vice president of the chamber of commerce; commissioned a captain in the medical corps, Army of the United States, on May 21, 1942; began active duty on June 22, 1942; later promoted to major; killed in action in the European area August 29, aged 43.

residency at the University Hospital; died August 19, aged 38, of bronchogenic carcinoma with metastasis.

Lovic Culver Ellis, Florence, Ala.; University of Tennessee College of Medicine, Memphis, 1914; member of the Medical Association of the State of Alabama; died September 22, aged 53, of coronary thrombosis.

Charles Henry Herrick, Unadilla, N. Y.; Albany Medical College, Albany, N. Y., 1893; member of the Medical Society of the State of New York; health officer of the village and town of Unadilla; formerly health officer of Gilbertsville; on the staff of the Sidney Hospital, Sidney; died in the Aurelia Osborn Fox Memorial Hospital, Oneonta, August 30, aged 80, of arteriosclerotic heart disease.

George Inglis, Oswego, Ore.; Rush Medical College, Chicago, 1884; died August 28, aged 88, of arteriosclerosis and myocarditis.

Roy Howard Johnson, Los Angeles; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1904; member of the California Medical Association; anesthetist at the Orthopaedic Hospital; member of the staff of the California Hospital, where he died July 24, aged 66, following a gastrectomy and virus pneumonia.

Charles Warton Kidder, Woodstock, Vt.; University of Vermont College of Medicine, Burlington, 1907; served during World War I; died in the Veterans Administration Facility, White River Junction, August 6, aged 59, of cerebral hemorrhage.

Franklin Jacob Lins, Durand, Ill.; Rush Medical College, Chicago, 1897; died in St. Anthony's Hospital, Rockford, August 1, aged 80, of coronary sclerosis.

Eugene Alphonsus McCabe, Sioux City, Iowa; John A. Creighton Medical College, Omaha, 1920; died August 21, aged 47, of coronary heart disease.

William Adam Mess ✦ Washington, D. C.; George Washington University School of Medicine, Washington, 1907; also a pharmacist; medical examiner for Selective Service Board number 14; on the staffs of the Sibley, Doctors, Homeopathic, Providence, Garfield, Georgetown, George Washington and Emergency hospitals; killed in an automobile accident on the Mount Vernon Highway, Alexandria, Va., August 11, aged 62.

Elmer Ewell Owen, Batavia, N. Y.; University of Michigan Homeopathic Medical School, Ann Arbor, 1907; member of the Medical Society of the State of New York; served in France during World War I; died August 2, aged 62, of actinomycosis.

Peter Marius Pedersen ✦ Dannebrog, Neb.; University of Nebraska College of Medicine, Omaha, 1904; died August 2, aged 73, of heart disease.

John Henry Reichling ✦ Bennington, Vt.; University of Vermont College of Medicine, Burlington, 1906; on the staff of the Henry W. Putnam Memorial Hospital; died in St. Donat, Canada, September 18, aged 65, of cardiac syncope.

Charles William Smith, Aliquippa, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1906; member of the Medical Society of the State of Pennsylvania; examining physician for draftees during World Wars I and II; served as president of the local board of health; died August 2, aged 66, of carcinoma of the left kidney.

Arthur Gilman Tullar ✦ North Hollywood, Calif.; Northwestern University Medical School, Chicago, 1906; died October 11, aged 67, of coronary thrombosis.

John David Vedder, Johnstown, N. Y.; Albany Medical College, Albany, N. Y., 1896; member of the Medical Society of the State of New York; served as secretary, president and treasurer of the Fulton County Medical Society; formerly city health officer, city physician and member of the board of health; on the courtesy staff of the Nathan Littauer Hospital, Gloversville; died August 7, aged 81, of pyonephrosis.

George Fritz Way ✦ Urbana, Ill.; University of Illinois College of Medicine, Chicago, 1911; died in the Wesley Memorial Hospital, Chicago, August 14, aged 59, of carcinoma of the rectosigmoid.

Carl Frederick Weinberger, Chicago; Rush Medical College, Chicago, 1907; member of the Illinois State Medical Society; at one time principal of Muskegon High School, Muskegon, Mich.; on the consulting staff, Evangelical Hospital of Chicago, where he died August 14, aged 71, of cerebral hemorrhage.

Jacob Andrew Youngman ✦ St. Louis; St. Louis College of Physicians and Surgeons, 1905; on the staff of St. Anthony's Hospital; died at his home in Sappington, Mo., August 10, aged 66, of coronary sclerosis and chronic myocarditis.

DIED WHILE IN MILITARY SERVICE

John Weyman Davis, Athens, Ga.; Emory University School of Medicine, Atlanta, 1927; member of the Medical Association of Georgia and the Southeastern Surgical Congress; fellow of the American College of Surgeons; on the surgical staffs of the Athens General and St. Mary's hospitals; commissioned a lieutenant commander in the medical corps of the U. S. Naval Reserve on Oct. 12, 1939; began active duty on May 19, 1941; promoted to commander on Aug. 1, 1942; died in the Naval Hospital, Charleston, S. C., September 18, aged 42, of Rocky Mountain spotted fever.

Frank John Fischer ✦ Chagrin Falls, Ohio; University of Wisconsin Medical School, Madison, 1934; formerly an intern and resident in surgery at the City Hospital and a resident in surgery at St. John's Hospital, both of Cleveland; fellow of the American College of Surgeons; served on the surgical staff of St. Luke's Hospital in Cleveland; certified as a commercial pilot by the Civilian Aeronautics Commission on July 1, 1942; commissioned a captain in the medical corps, Army of the United States, on Sept. 8, 1942; certified as an aviation medical examiner; stationed at the hospital, Camp Springs, Army Air Field, Washington, D. C.; died September 21, aged 35, as the result of a plane crash following a forced landing 20 miles west of Leesburg, Va.

John Edward Fissel Jr., Newport News, Va.; University of Maryland School of Medicine, College of Physicians and Surgeons, Baltimore, 1936; formerly secretary and treasurer of the Warwick County Medical Society; served an internship at the Church Home and Infirmary in Baltimore and a residency in surgery at the Riverside Hospital; commissioned a first lieutenant in the medical reserve corps of the U. S. Army on Sept. 7, 1942; later promoted to captain; killed in Prestewick, Scotland, August 22, aged 32, in an airplane accident.

Frederick Hugh Greenwell, Lieutenant (jg) M. C., U. S. Navy, New Haven, Ky.; University of Louisville (Ky.) School of Medicine, 1943; intern at the Naval Hospital, Jacksonville, Fla., where he died August 10, aged 25, of primary atypical pneumonia.

George Bernhard Miller ✦ San Francisco; Stanford University School of Medicine, San Francisco, 1935; served an internship and residency at the Lane and Stanford University Hospitals and a residency in tuberculosis at the San Francisco Hospital; commissioned a first lieutenant in the medical corps, Army of the United States, on Nov. 11, 1942; died in Grass Valley July 15, aged 34, of myocardial infarction due to coronary disease.

Woodman Bradbury Pomeroy ✦ Lieutenant, M. C., U. S. Navy, Pittsburgh; Harvard Medical School, Boston, 1941; served an internship at the Pittsburgh Medical Center; commissioned a lieutenant (jg) in the medical corps, U. S. Navy, on July 14, 1942; promoted to lieutenant on May 1, 1943; flight surgeon; died in the Pacific area July 12, aged 28, of extensive multiple injuries.

Stephen William Smith Jr., Hamden, Conn.; Tufts College Medical School, Boston, 1940; served an internship at the Memorial Hospital in Worcester, Mass.; diplomate of the National Board of Medical Examiners; commissioned a lieutenant (jg), medical corps, U. S. Naval Reserve on Nov. 4, 1941; later assigned to the destroyer U. S. S. *Ingraham*; promoted to lieutenant on June 15, 1942; aged 28; presumptive date of death at sea in the Atlantic area, Aug. 23, 1943, according to the Navy Department.

Jerome Daniel Solomon, Chicago; University of Illinois College of Medicine, Chicago, 1941; served an internship at the Cook County Hospital; commissioned a first lieutenant in the medical reserve corps of the U. S. Army on June 6, 1941; began active duty on Sept. 21, 1942; later promoted to captain; died in the Southwest Pacific area September 16, aged 28, of tsutsugamushi fever and malaria.

John Wesley Speake Jr., Spartanburg, S. C.; Medical College of the State of South Carolina, Charleston, 1936; served an internship at the Spartanburg General Hospital; commissioned a first lieutenant in the medical corps, Army of the United States, on Aug. 12, 1942; later promoted to captain; a flight surgeon; killed in the European area July 28 in an airplane accident, aged 34.

Bureau of Investigation

ADVENTURES OF A DODGER

"Oh Boy!" Perry's Scheme Declared a Mail-Order Fraud

Many of those who dispense health hokum to a credulous public might prosper indefinitely in their enterprises, did not a skeptical Post Office Department look into their schemes and scotch them with fraud orders. Such was the case of Victor Edison Perry of Philadelphia, who carried the letters N.D. after his name, indicating that he is either a naturopath or a naprapath.

In January 1943 the Post Office Department cited Perry to appear at a hearing and show cause why his business should not be debarred from the mails on the charge that it was a scheme to obtain money through the sale of "GEN SEN" under fraudulent representations that it was an effective treatment for arthritis, diabetes, asthma, liver, kidney, bladder and stomach disorders, and some other ailments. Perry then signed an affidavit that his business had been absolutely discontinued and would not be resumed at any time under any name. This affidavit, he admitted, was filed for the purpose of obviating future fraud order proceedings. In it he agreed to acquiesce to such fraud order if he should be found to have violated his promise. And violate it he did. He continued his business, substituting the names "Vita" and "Nu-Vita" for the old one, "GEN SEN," adopting the new trade styles "Vita Herbs Company," "Nu-Vita Herbs Company" and "V. E. Perry" and using New York and Philadelphia addresses. Soon afterward he executed another affidavit for the Post Office Department, in which he admitted that he had resumed the sale of his nostrum under the aforesaid new names, thus violating the earlier affidavit. In this second one he again declared that his enterprise had been absolutely discontinued and would not be resumed. In November 1943, however, the Post Office Department cited him again to show cause why a fraud order should not be issued against him. The outcome of the hearing will be mentioned later.

Perry's penchant for alliteration in calling certain of his later nostrums "Perry's Peptone Pep Pills," "Peptone Perry's Pink Pep Pills" and "Perry's Famous Peptone (Spanish Fly) Pep Pink Pills" recalls another medicaster's "Pink Pills for Pale People." As the names indicated, the various "Pep Pills" were promoted for sexual weakness. Another Perry nostrum, "Natura," was represented as a cure for rheumatism, catarrh, low or high blood pressure, swollen tonsils and many other disorders. Perry advertised all his nostrums in their time through periodicals of local and national circulation. What he formerly sold as GEN SEN was played up as "God's gift to India and India's gift to you," and also as "India's Famous Herb Tea." It consisted of three units which were contained, respectively, in red, white and blue packages carrying the American flag (an apparent violation of law), and prospective customers received return envelopes addressed to Perry, on which he spelled his first name "Victory." Some of his advertising literature carried a large red heart on which was printed in white "Is your wife still your sweetheart?- Try GEN SEN."

The advertising of Natura, instead of representing the product as being from India, described it as a "Mexico herb tea," and this literature, too, was done in red, white and blue. If one could believe the claims, it was the "World's Greatest Spring Tonic" and would help "hubby and yourself over 30" feel like "Sweet Sixteen . . . Oh Boy!" Besides, it was touted as a reducer under the slogan "It's so easy to be streamline, with Natura."

This "streamliner," according to a government chemist who testified at the Post Office hearing, contained sulfur, epsom salt, sodium bicarbonate, senna, cascara and licorice and was identical with GEN SEN. Perry's Peptone Pep Pills, the witness said, were essentially a mixture of gentian, phosphorus, strychnine, yohimbin, iodine, cantharides and U. S. P. thyroid. None of the ingredients named for the two preparations constituted anything original or unfamiliar, as was pointed out by another government witness, a Senior Medical Officer of the Food and Drug Administration, nor would such mixtures have any particularly beneficial effect on the ailments for which these were advertised. He showed that they would not purify the blood or restore the user to a "new life of youth and pep," nor would Natura be of any value whatever in treating obesity. As for impotence, he testified, the only proper treatment for this would have to be based on a careful diagnosis to ascertain the type and cause of the condition, which in some cases might be psychic.

At this hearing Perry offered no medical witness but, when given opportunity to present his case, devoted practically all his time to asserting that the use of his preparations had given him the vigorous health that was his despite his seventy-seven years. The charges against him were sustained by the evidence presented, and on May 12, 1944 a fraud order was issued, covering the names Victor Edison Perry, Victory Edison Perry and the numerous variations that he used.

Reproduced on this page is the carton front of another Perry nostrum, apparently a supplementary laxative, "Natura (Ovato Seeds)." On another side of the carton is the claim "Ovato Seeds . . . from Mother Earth — Contains the 16 Elements of Health," and the further boast "Prominent M.D.'s all over, also Metropolitan Life Insurance Co., N. Y. Life Extension Institute and U. S. Government recommend it very highly." The package also bears the name of the National Health University (whatever that may be), designating Perry as its president and giving addresses in New York, Boston and Worcester, Mass., besides mentioning "Operating 23 Founts of Youth, Pep, Beauty, Health, $ucce$$ in U. S. A." Possibly one of the "Founts" was "Dr. Perry's Famous Water Crystal and Mineral Salt Hotel and Baths," which, a report said, he was once operating in Beaumont, Texas. The same report stated that his National Health University had its main "laboratory" at Burbank, Calif., and that Perry gave "lectures" to promote the sale of many types of alleged health foods.

OPEN THIS END
DON'T SPILL — IT'S PRECIOUS!
A FOOD FROM HEAVEN FOR SUFFERING HUMANITY
GOOD-BYE, DOCTORS! — USE
NATURA — (Ovato Seeds)
THE ONLY HARMLESS REMEDY FOR CONSTIPATION
NATURE'S NEW LAXATIVE, A FOOD, NOT A DRUG!
Victor Edison Perry
PRESIDENT
NATIONAL HEALTH UNIVERSITY
Main Office: 1560 Broadway, N. Y. C.
GOD'S Great GIFT to NATURE
Nature's great Gift to Humanity
Not Genuine
Without My Photo
and Signature
PRICE, $1.00

Carton front of "Natura (Ovato Seeds)."

Apparently the activities of Victor Edison Perry, national dispenser of health, can best be summarized by a term in his own advertising—"Oh Boy!" But he is now seventy-seven years old and if Post Office fraud orders won't stop him, the biologic life cycle probably will.

Correspondence

MALIGNANT GROWTH AFTER SINGLE TRAUMA

To the Editor:—As a contribution toward the solution of the problem raised by correspondents in THE JOURNAL, September 9 and 16, concerning the possibility of a malignant growth resulting from a single trauma, I submit the following case report. Please note that it is based on the sworn testimony of physicians and others having personal knowledge of the facts of the case reported:

In April 1935, about 11 p. m., in Salina, Kan., Parker, in the course of his employment, was carrying a box of books. He stumbled, the box struck and damaged the top of a desk, and Parker's chest struck the box. Before quitting work, about 1 a. m., Parker left a note for his supervisor reporting the incident. Whether he reported at that time that he had been hurt is not clear, but when he reached home shortly after 1 o'clock he told his wife of the accident and that his chest had struck the box and was hurting. There was no evidence that he had up to that time suffered from any chest pain. His wife did not examine his chest until three or four weeks later. Then she found "a red spot" about the size of a dollar. On May 15 Parker consulted a physician. About the same time—possibly a month or six weeks or possibly two months after the accident—he told his supervisor that he had hurt his chest when he fell with the box of books and that "a bump" on his chest was caused by a bump or a bruise. Two weeks later, admittedly six weeks to two months after the accident, he showed his supervisor "the swelling" and told him that he got it when he dropped the box about two months previously. Parker continued at work for about fourteen months, although under the care of a physician, Dr. Jenney. By June 16, 1936 the tumor had grown to a lump "the size of a baby's head." It was then removed by an operation. Thereafter Parker was confined to his bed until his death, Sept. 16, 1936.

In proceedings by Parker's widow under the workmen's compensation act, four physicians testified. Dr. Jenney, who had treated Parker from about three weeks after his injury until the time of his death, testified that when Parker first came to his office he had "a hard protuberance, tumor-like" and that he, Jenney, believed that the fall and hurt of which Parker told him was the cause of the injury that eventually developed into the sarcoma of the breastbone. Dr. Fitzpatrick, who had taken x-ray pictures of Parker's chest in March 1936, testified that they revealed a growth on the chest and bone, destruction of the sternum and cartilage of the ribs in the front of the chest; he gave it as his professional opinion that Parker's condition could have possibly come from the alleged injury to his chest in 1935. Dr. Mowery, who removed the growth, gave it as his professional opinion that the tumor resulted from the injury. Dr. Seit, an expert called not by the claimant but by the respondent, testified that sarcoma malignancies are not traceable to trauma in more than two percent of the cases, or even less, but he added:

> The important thing is the establishment of the fact of a trauma, and finding within this tissue or that immediately adjacent to the . . . periosteum and the structure of the bone or immediately adjacent to the point of the alleged injury, evidence of the injury. If in such a tissue anywhere from four weeks to a year, or even more, a malignancy develops, I believe it would be considered due to the trauma.

The foregoing clinical history is summarized from a decision of the Supreme Court of Kansas, Dec. 11, 1937, in *Parker, appellee,* v. *The Farmers Union Mutual Insurance Company and The Maryland Casualty Company,* 146 Kan. 832 (73 P. 2d, 1032). In summarizing the evidence, the court said:

> . . . shall this court say that Parker's prompt report to Cameron, his superior, about his tripping and falling with the box of books, his later statement to Cameron that he hurt his chest in the same fall, the rapid growth of the malignant tumor on his breastbone and the professional opinions of the doctors that such a malignant growth was probably due to the injury as narrated by Parker—all these evidential matters, including the pertinent circumstances, were not sufficient to establish the fact of the accident and the injury? How could the evidence be stronger?

Was not the injury described the exciting cause of the sarcoma that followed? Before denying a causative relation one should point out some reasonably likely cause other than the injury. Before attributing the entire incident to the so-called laws of chance, one should consider the incidence rates of sarcomas of the sternum and of contusions of the sternum on the entire population and then estimate the chances of the occurrence of such a contusion and such a sarcoma coincidentally in site and in immediately chronological sequence. If it be admitted that a contusion has ever caused a sarcoma of the sternum, what ground is there for believing that other traumas may not cause other malignant growths? The relation between malignant growths and cleancut incised wounds and punctured wounds made with sharp instruments may merit separate consideration, for I cannot recall ever seeing a report of a claim for compensation based on the occurrence of a malignant growth as the result of such an injury. Even so, one must not overlook the etiology of keloids, sometimes attributed to even such trauma.

A large financial interest is involved in the problem here discussed. An employee who suffers from a malignant growth caused by a trauma arising out of and in the course of his employment is in most jurisdictions, if not in all, entitled by law to compensation for the injury, to be paid by the employer by whom he was employed when the injury was received. The presence of such a growth at the site of the injury cannot enter into the determination of compensation if the element of causation is not proved. Proof need not be conclusive or beyond a reasonable doubt. The award is made according to the preponderance of the weight of the evidence submitted by employee and employer. If a single trauma can never by any possibility cause a malignant growth, however, every award in favor of the employee in such a case obviously imposes an injustice on the employer, no matter what the weight of the evidence may be.

To prevent such injustice it has been urged that the dictum which denies the possibility of a causative relation between any single trauma and a malignant growth subsequently appearing on the site of that trauma be generally accepted. The universal acceptance of that dictum would go a long way toward preventing such injustice. But might it not give rise to injustice equally extensive and even more grave? It would certainly tend to deter injured workmen from filing claims based on such injuries and growths, hinder lawyers in the prosecution of such claims, embarrass physicians, regardless of their own studies, experience and observation, sought as witnesses in support of such claims, and operate, subconsciously or otherwise, to warp the judgments of boards, commissions and courts required to pass judgment. For possible injustice to individual employers, the adoption of the dictum of noncausation would substitute certain mass injustice to many employees, if it should prove unfounded, as the case stated at the beginning of this communication indicates that it is. And by the time the fallacy of the dictum was demonstrated many employees, and many persons in other walks of life who but for it might have sought damages for injuries suffered at the hands of others, will have lost their rights to redress, through the limitations of time for presenting their claims fixed by the workmen's compensation acts and statutes of limitation and through the disappearance of essential witnesses.

Have biology and medical science already determined the causes of malignant growths in the human body so certainly as to call for affirmative action to cause the adoption universally of the dictum that no single trauma ever has caused a malignant growth or ever can do so? Do available records indicate that under existing medical and legal procedure so many employers are being unjustly required to pay compensation for malignant growths due to single traumas as to require a revision of medi-

cal opinion with respect to the cause or causes of such growths? If neither of these questions can be answered in the affirmative, why not wait for further evidence as to the causes that operate to produce such growths before undertaking to reform medical opinion?

WILLIAM C. WOODWARD, M.D., Washington, D. C.

"YAWS, CUTANEOUS LEISHMANIASIS AND PINTA"

To the Editors:—With reference to Dr. Howard Fox's communication (THE JOURNAL, April 8) replying to my comments (March 4) regarding his article "Yaws, Cutaneous Leishmaniasis and Pinta" (THE JOURNAL, Oct. 23, 1943) I should like to point out:

1. If an incidence of 4 per cent of the macular rash of yaws is considered "the equivalent of being nearly always absent," then we are in agreement as to this type of lesion. As the macular rash appears early in the course of the disease its incidence should be calculated on the total number of lesions of all types seen in persons with a history duration of one year or less. My calculations on this basis gave an incidence of 6.5 per cent. Either figure (4 or 6.5 per cent) seems to me significant, particularly as in some cases there may be only a few macules and the tendency is for them to disappear early—perhaps before the patient comes up for examination. For purposes of comparison I should be glad to know what, in the experience of others, is the incidence of the roseola rash of syphilis.

2. In support of his statement "In the early stages the disease may be permanently cured by three successive injections of neoarsphenamine," Dr. Fox mentions the results of Morse, quoted by Strong, on 1,064 cases treated in Santo Domingo (in my edition Stitt Moss is quoted) and revisited after five years. Moss (again in my edition) found that 46.5 per cent of the cases reexamined—i. e., 419—remained uncured. He also quotes Strong to the effect that in the Philippines with two injections as the rule 94.3 per cent of clinical cures resulted. No mention is made of the period over which these cases in the Philippines were followed up or if by the term "clinical cure" a temporary clearing up only of the lesions is meant.

I quoted in my previous article the percentages of persistent positive Wassermann reactions at six, twelve and eighteen months in a series of 411 cases in which six successive injections of neoarsphenamine had been administered. I should have added that it was from these persistent positive reactions the relapsing lesions developed; that infectious relapsing lesions were more frequent during the first year following treatment of early cases than in the second or subsequent years; that environmental and climatic conditions were major factors in determining the time and percentage of relapses (consequently patients should be revisited in their districts toward the end of the rainy seasons to determine the real effects of treatment—an important point).

In a small series of 209 persons treated with four to six injections of neoarsphenamine (average 5.5 injections per patient) and revisited at six, twelve, eighteen and twenty-four months later, 28 had relapsing lesions (6 after six months, 7 after twelve, 9 after eighteen and 6 after twenty-four), a percentage of 13.4 relapsing cases. This percentage was found to be still higher for patients receiving one to three injections. Cases may relapse repeatedly in spite of an additional two to three injections after each relapse. The figure 28 represents the number of first relapses; further relapses are not included.

On the other hand, before an estimate can be made of the results of treatment there should be a clear picture as to the course of the disease in cases in which treatment has never been given. In Jamaica active lesions attributable to yaws are quite rare in patients who give a history of yaws of thirty or more years' duration.

Moss revisited his 1,064 patients in Santo Domingo after a period of five years. In two areas in Jamaica 1,520 persons with a history of yaws of five years upward who maintained that they had never had treatment by injections were seen and 1,424, or 93.65 per cent, showed no clinical evidence of active yaws; only 96, or 6.64 per cent, had such evidence. In these same areas 467 patients gave a history of yaws of four years or less without receiving treatment; 308, or 65.95 per cent, had active yaws lesions; 159, or 34.05 per cent, had no active lesions.

My contention is that specific treatment early in the course of the disease is of value primarily in limiting the spread of the disease in any community where environmental conditions cannot be speedily improved. Such treatment (even with six or more injections) does not necessarily indicate that the disease is cured. I would suggest that to regard the absence of physical lesions as evidence of cure is no more logical than to do so in cases of syphilis.

It would be comparatively easy to clear endemic areas of yaws if one to three injections could cure the disease. The fact is that there will always be some cases of relapsing infectious lesions from which a further spread of the disease by contagion is possible.

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General Hospital,
Kingston, Jamaica.

[The letter was referred to Dr. Fox, who replies:]

1. Dr. Chambers has made it appear that I considered a 4 per cent incidence of the macular eruption to be the equivalent of being "nearly always absent." In my answer to his communication in THE JOURNAL, April 8, I distinctly said that only one author had observed such an incidence. All others of long experience with yaws either failed to mention a macular eruption or definitely said that it did not occur in yaws.

2. The statement quoted from Colonel Strong was to the effect that in the early stages the disease *may* (italics mine) be permanently cured by three successive injections of neoarsphenamine. This would not mean that such a result was always bound to occur.

Dr. Chambers said that in his own series of 209 cases treated by an average of 5.5 injections of neoarsphenamine he found 13.4 per cent of relapses after periods of observation varying from six to twenty-four months. The freedom from relapse in 86.6 per cent of his cases supports my opinion of the curability of yaws in the early stages, certainly when compared with the curability of syphilis.

HOWARD FOX, M.D., New York.

PRIZE WINNING MONOGRAPHS IN BRAZIL

To the Editor:—In THE JOURNAL, May 6, a mistake was noted in the letter from Brazil. The monographs are in error, since separate competitions were entered during the year, and the following is a correct listing of the prize winning monographs:

1. "History of Leprosy in Brazil and the Geographic Distribution of the Disease," by Flavio Maurano.

2. "Etiology and Pathology of Leprosy," by Abrahão Rotberg and Luiz Marino Bechelli.

3. "Epidemiology and Control of Leprosy," by Nelson Sousa Campos, Abrahão Rotberg and Luiz Marino Bechelli.

4. "Clinic and Therapeutic of Leprosy," by Luiz Marino Bechelli, Abrahão Rotberg and Flavio Maurano.

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Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Medical Practice Acts: Conviction of Limited Practitioner for Exceeding the Scope of His License.—The Bureau of Medical Education and Licensure of Pennsylvania [1] in 1915 issued a limited license to Allison which conferred on him "the right to treat the sick by Herbs and Massage . . . upon request of a person duly authorized to prescribe the same." Twice previous to the institution of the action here involved he was convicted of having exceeded the authority granted him by this license and of engaging in the practice of medicine and surgery. Both convictions were upheld by the superior court of Pennsylvania. *Commonwealth* v. *Allison,* 103 Pa. Superior 140, 156 A. 812; id. 132 Pa. Superior 606, 1 A. (2d) 920. Again, in the case here abstracted, he was indicted for and convicted of exceeding the scope of his limited license and engaging in the practice of medicine and surgery without restriction. He appealed to the superior court of Pennsylvania.

Either Allison, said the superior court, has no respect for the law or he is mentally incapable of understanding the limitations implicit in the form of license he possesses. For not only did the prosecution show that, at the times charged in the indictment, he accepted patients, examined them, diagnosed their ailments and prescribed treatments; he glibly admitted these practices from the witness stand. And there is not even the pretense that he limited his patients to those referred for treatment by a properly licensed physician; in fact, one has the impression from reading his testimony that he regards all orthodox physicians as either fools or knaves and will have little or nothing to do with them. Having twice appealed to us in vain one would expect that in this, his third, appeal the ingenuity of counsel, challenged by almost overwhelming odds, would produce a somewhat novel approach to the problem. We have not been disappointed. Allison now contends that, in restricting him to the treatment of patients referred to him by licensed physicians, the licensing agency—composed, according to him, of "professional competitors"—has arbitrarily discriminated against him; that there is no statutory authority in Pennsylvania for such a narrow limitation on his authority and that the limitation contravenes the Fourteenth Amendment to the Federal Constitution.

True, continued the court, there is no express statutory authority for the particular limitation complained of by Allison. The Pennsylvania medical practice act gives the bureau broad, discretionary powers to establish a system of special licensure and to issue to persons who fulfil such special qualifications as the bureau provides a license to practice one or more of the limited branches of medicine or surgery. The constitutionality of this provision was unheld in *Long* v. *Metzger,* 301 Pa. 449, 152 A. 572. Of necessity the bureau may make discriminations; they are inherent in the nature of the functions it performs. Yet we must grant that the acts of the bureau may always be subjected, by one affected, to the test of reasonableness under the Fourteenth Amendment. But, so far from being unreasonable, the requirement imposed by the bureau that practitioners of this kind should treat patients only at the request of, and hence under some supervision by, a licensed physician is a necessity if the public is to be protected adequately against exploitation.

Allison, continued the superior court, is a quack of the worst sort. It is easy to see why, if he were compelled to wait for patients referred to him by physicians, he would have no practice. At the trial there was no proof of the chemical ingredients of the pills and nostrums he sold to his patients nor the type of massage he employed. But the miracles he professed to be able to accomplish would make the witchery of the Middle Ages seem by comparison an infant and underdeveloped craft. He professes to be a "bloodless surgeon, a botanic physician." When asked how he would cure a case of appendicitis he said:

> That is very easy. That would be cured in one hour's time ordinarily without shedding any blood or making any incision or like that. That is easily cured in one hour and a patient is ready to go to work in one hour.

When asked what he would do with ruptured appendix, he said:

> Why, my friend, I have been practicing forty-three years and I have yet to see the physician that has ever saw [sic] a ruptured appendix.

He could remove diseased tonsils without cutting:

> By the use of herbs taken internally and massage to the throat, cure any case of tonsils, just—well, I'll say within a week or so.

He professed to have cured many cases of cancer, and as for paralysis:

> Often times paralysis is caused by an obstruction of circulation and by removing that obstruction in a few minutes time the party has the full use of their arms or legs.

It makes one shudder, continued the court, to think that a man like this should be entrusted with any part of the responsibility for the diagnosis or treatment of human disease. The story of this case is more persuasive than any abstract argument could possibly be of the wisdom of the bureau in limiting such practitioners to treatments requested by licensed physicians.

Accordingly, the judgment of conviction was affirmed.—*Commonwealth v. Allison, 38 A. (2d) 535 (Pa., 1944).*

1. Now officially designated as the State Board of Medical Education and Licensure.

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

BOARDS OF MEDICAL EXAMINERS BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Examinations of boards of medical examiners and boards of examiners in the basic sciences were published in THE JOURNAL, Nov. 4, page 656.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Parts I and II. Various centers, Nov. 13-15. Exec. Sec., Mr. E. S. Elwood, 225 S. 15th St., Philadelphia.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY: New York, June 8-9. Final date for filing application is March 12. Sec., Dr. George M. Lewis, 66 E. 66th St., New York 21.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* Feb. 19. Final date for filing application is Dec. 15. Asst. Sec., Dr. W. A. Werrell, 1301 University Ave., Madison 5, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: Spring. Final date for filing application is Feb. 1. Sec., Dr. Paul C. Bucy, 912 S. Wood St., Chicago 12.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Written. Part I.* Various centers, Feb. 3. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh 6.

AMERICAN BOARD OF OPHTHALMOLOGY: New York, June, Chicago, October. Final date for filing application is Dec. 1. Sec., Dr. S. Judd Beach, 56 Ivie Road, Cape Cottage, Maine.

AMERICAN BOARD OF OTOLARYNGOLOGY: New York, June 5-8. Chicago, Oct. 3-6. Sec., Dr. Dean M. Lierle, University Hospital, Iowa City, Ia.

AMERICAN BOARD OF PEDIATRICS: *Oral.* New York, April 14-15. Final date for filing application is Dec. 15. Chicago, May 19-20. Final date for filing application is Jan. 19. Sec., Dr. C. A. Aldrich, 115½ First Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF RADIOLOGY: *Oral.* New York, June 3. Final date for filing application is May 1. Sec., Dr. B. R. Kirklin, 102-110 Second Ave. S.W., Rochester, Minn.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1934 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Diseases of Children, Chicago

68: 83-156 (Aug.) 1944

Clinical Adequacy of Single Measurement of Vitamin A Absorption. E. L. Pratt and Kathleen R. Fahey.—p. 83.
Group Psychotherapy for Withdrawn Adolescents. J. C. Solomon and Pearl L. Axelrod.—p. 86.
*Management and Prognosis of Megacolon (Hirschsprung's Disease): Review of 24 Cases. K. S. Grimson, H. N. Vandergrift and H. M. Dratz.—p. 102.
Meningococcic Meningitis: Review of 100 Cases. K. Glaser.—p. 116.
Poliomyelitis: III. Analysis of Results Following Treatment as Reported in Recent Literature. J. A. Toomey and P. M. Kohn.—p. 124.

Management and Prognosis of Megacolon (Hirschsprung's Disease).—Grimson and his co-workers review the records of patients with megacolon seen since the opening of Duke clinic in 1930. The present status of the patients has been determined by correspondence and by return visits. Of 24 patients with megacolon, 21 were treated by conventional medical management, consisting chiefly of diet, laxatives, enemas and parasympathomimetics, occasionally supplemented by sympathectomy. Three of the 21 patients required emergency laparotomy. A severe fecal impaction was removed in 1. Volvulus of the sigmoid colon was reduced in 2. Six of the 21 patients have undergone a remission of symptoms without surgical intervention. One patient underwent a remission of symptoms after sympathectomy and is well at the age of 17. Seven have continued to have mild to severe symptoms and at an average age of 15 are receiving medical treatment. Five patients, including 1 of the 3 who had a laparotomy, have died. The remaining 3 of the 24 patients presented alarming symptoms and were treated by one stage resection of the megacolon and ileosigmoidostomy. These 3 are now living and well. Medical management was supplemented by sympathectomy for 4 of the 24 patients. The gross pathologic picture was not significantly altered. One sympathectomized patient improved and is living and well at the age of 17. Another improved for three years and then died at the age of 24 with an acute impaction and perforation of the colon. Two others experienced difficulty after sympathectomy. The initial observations indicate three types of involvement of the colon, and the follow-up studies warrant classification of the 24 patients into three groups. The first group, of 12 patients, had uniform involvement of the entire colon terminating in a dilated or easily dilatable rectum. Eight are now living and evacuating their colons readily. It appears that protracted medical management of patients in this group is indicated as long as adequate nutrition can be maintained and persistent abdominal distention avoided. The 7 patients of group 2 had uniform dilatation of the proximal segments of colon terminating in a normal segment of bowel, usually in the sigmoid region, and a normal rectum. Four receiving conventional management died. The remaining 3, with enormous megacolons, were treated by resection of the megacolon and anastomosis between the terminal portion of the ileum and the remaining stump of normal sigmoid colon. These 3 are living and well. Patients in this group demonstrated greater abdominal enlargement than the other patients. The third group comprised 5 patients who had enormous enlargement of the sigmoid colon or of the sigmoid and descending colon, with or without involvement of the proximal portions of the colon and of the rectum. The 5 are now living, 2 free from symptoms and 3 with moderately severe symptoms. It seems that protracted medical management of patients in this group is justified.

American Journal of Physiology, Baltimore

142: 1-152 (Aug.) 1944. **Partial Index**

Design of Ballistocardiograph. J. L. Nickerson and H. J. Curtis.—p. 1.
Study of Substances in Blood Serum and Platelets Which Stimulate Smooth Muscle. Marjorie Bass Zucker.—p. 12.
Rate of Entrance of Radio Sodium into Aqueous Humor and Cerebrospinal Fluid. M. B. Visscher and C. Carr.—p. 27.
Influence of Temperature on Spinal Cord Damage Caused by Asphyxiation. A. van Harreveld and D. B. Tyler.—p. 32.
Hemoglobin Concentration of Blood of Intact and Splenectomized Dogs Under Pentobarbital Sodium Anesthesia, with Particular Reference to Effect of Hemorrhage. D. T. Carr and H. E. Essex.—p. 40.
Augmentation of Left Coronary Inflow with Elevation of Left Ventricular Pressure and Observations on Mechanism for Increased Coronary Inflow with Increased Cardiac Load. D. E. Gregg and R. E. Shipley.—p. 44.
Respiratory Effects on Filling of Ventricles During Prolonged Diastole. Mary C. Patras, J. M. Brookhart and T. E. Boyd.—p. 52.
Tissue Electrolyte at Low Atmospheric Pressures. D. C. Darrow.—p. 61.
Depression of Normal Erythrocyte Number by Soybean Lecithin or Choline. J. E. Davis.—p. 65.
Palmar Skin Resistance During Standard Period of Controlled Muscular Activity as Measure of Physical Fitness and Fatigue. A. H. Ryan and E. L. Ranseen.—p. 68.
Maintenance of Normal Serum Calcium by Parathyroid Gland in Nephrectomized Dogs. E. P. Monahan and S. Freeman.—p. 104.
Synergistic Effect of Caffeine on Histamine in Relation to Gastric Secretion. J. A. Roth and A. C. Ivy.—p. 107.
Sensitivity of Respiratory Center to Hydrogen Ion Concentration. M. G. Banus, H. H. Corman, V. P. Perlo and G. L. Popkin—p. 121.
Energy Expenditure in Swimming. P. V. Karpovich and N. Millman.—p. 140.
Radioactive Phosphorus Studies on Hexosemonophosphate Metabolism in Resting Muscle. J. Sacks.—p. 145.

Am. J. Syphilis, Gonorrhea and Ven. Dis., St. Louis

28: 529-660 (Sept.) 1944

Review of 2,144 Courses of Rapid Treatment for Early Syphilis. E. W. Thomas and Gertrude Wexler.—p. 529.
*Intensive Chemotherapy of Early Syphilis. A. W. Neilson, L. F. Blaney, L. J. Stephens and R. W. Maxwell.—p. 553.
Contact Investigation in Gonorrhea. N. W. Guthrie.—p. 571.
Syphilis in Gonorrhea Patients and Contacts. N. W. Guthrie.—p. 583.
*Polyarticular Arthritis and Osteomyelitis Due to Granuloma Inguinale. J. Lyford III, R. B. Scott and R. W. Johnson Jr.—p. 588.
*Penicillin in Treatment of Granuloma Inguinale. R. A. Nelson.—p. 611.
Enhancement of Virulence of Gonococcus for Mouse. C. P. Miller, with technical assistance of E. Tamani.—p. 620.
Susceptibility of Sulfonamide Resistant Gonococci to Penicillin. A. W. Frisch, with technical assistance of Beatrice Behr, R. B. Edwards and M. W. Edwards.—p. 627.
Statistical Studies in Female Gonorrhea with Evaluation of Yeast Supplement in Gonococcus Isolation. P. Rosenblatt, Edda Myer and Lillian Robbins.—p. 634.

Intensive Chemotherapy of Early Syphilis.—The treatment routine used by Neilson and his collaborators at Isolation Hospital in St. Louis was that devised by Chargin; 240 mg. of mapharsen was given daily for five consecutive days, totaling 1,200 mg. The daily dose of drug was given in 2,000 cc. of 5 per cent glucose solution dripped intravenously over a twelve hour period. Because fatalities resulted in small persons, the total dose for persons weighing less than 125 pounds (57 Kg.) was reduced to 900 mg. The 5 per cent glucose solution was later replaced by a 10 per cent solution, and the daily administration time was reduced from twelve hours to eight hours. Intensive therapy was completed 502 times on 487 patients. A few individuals were rejected because of a history of sensitivity to arsenic. In over one half of the cases, insoluble bismuth was given in an attempt to create a chemotherapeutic regimen of maximum effectiveness. The authors describe and evaluate early and delayed reactions and discuss the 4 fatalities. Thirty-seven per cent of the first 414 patients receiving intensive therapy failed to make a single contact with the follow-up clinic. The time interval between treatment and the achievement of a negative Kahn test averaged 4.3 months in the group receiving mapharsen alone and 2.8 months in the group that received a bismuth compound in addition to mapharsen. Fifteen per cent of all patients followed for five months or longer developed serologic or mucocutaneous relapse. Many of these were given a second course of intensive treatment. Twenty pregnant women were treated and 17 were followed until delivery had occurred. Only 2 infants had definite congenital syphilis, and 2 babies had positive Kahn reactions. The follow-up of treated patients has not yet been long enough for a proper evaluation of the results. The authors believe that the rate of complete cure will not be less than 70 per cent.

Arthritis and Osteomyelitis Due to Granuloma Inguinale.—Lyford and his associates reported previous observations on a case of disseminated granuloma inguinale with polyarticular arthritis and osteomyelitis in which the Donovan bodies were found on microscopic examination and were grown in continuous tissue cultures of material from the bone and joint lesions. They have also seen 2 cases of osteomyelitis (forearm and spine) in which the Donovan bodies were demonstrated in the lesions. In 1 case there was a systemic dissemination of the disease with a massive polyarticular arthritis and ultimately ulceration of many of the joints, and a widespread destruction of the bones. In another there was involvement of two vertebrae and a hip joint communicating with sinus tracts presenting in the inguinal regions. The third patient had lesions in the bones of a hand and forearm but no joint involvement. These cases add further proof that granuloma inguinale can be a systemic as well as a local disease. All patients showed persistent anemia and gradual loss in weight. All had irregular spiking temperatures over a long period of time. The activity of the lesions and the systemic manifestations were characterized by recurring espisodes of spontaneous remissions and exacerbations. The arthritis had an insidious onset with migratory pains in several joints and then swelling of several joints with pain locally but little free fluid. There was a slow subsidence into atypical "rheumatoid arthritis," followed by a recurrence of the acute swelling and pain of multiple joints, ending after many months in ulceration from within outward of many of the joints. Exploration of an elbow joint during the period of quiescence showed the synovia to be thickened and friable, but the articular cartilages were clean and smooth. The operative incision into the infected tissue of the joint healed by first intention and remained healed. The bone lesions on radiographic examination showed little or no sequestrum or involucrum formation and a lytic type of reaction. The lesions contained no pus and consisted of friable granulation tissue. Donovan bodies were seen in material from the bone and joint lesions in 2 cases and in material from the sinus tracts communicating with the involved bones in the third case.

Penicillin in the Treatment of Granuloma Inguinale.—Nelson administered penicillin to 2 patients with chronic granuloma inguinale. The diagnosis was proved in both cases by biopsy, which in each case showed Donovan bodies. One patient was given 1,360,000 Florey units of sodium penicillin by intramuscular injection in a period of four and one-half days; the other received 2,800,000 units during a fifteen day treatment course. No significant change was observed in the lesions in either patient in the following thirty to forty days. Donovan bodies were still present in the tissues of the first patient twenty-seven days after therapy was begun.

Archives of Internal Medicine, Chicago

74: 81-154 (Aug.) 1944

*Diabetes Insipidus: Clinical Observations in 42 Cases. G. M. Jones. —p. 81.
Disease of Mitral Valve: Its Effect on Pattern of Electrocardiogram. B. V. White, R. C. Parker Jr. and A. M. Master.—p. 94.
*Vasodepressor and Carotid Sinus Syncope: Clinical, Electroencephalographic and Electrocardiographic Observations. G. L. Engel, J. Romano and T. R. McLin.—p. 100.
Intestinal Malabsorption Associated with Tuberculosis of Mesenteric Lymph Nodes. A. Klein and W. B. Porter.—p. 120.

Diabetes Insipidus.—Jones reports 42 cases of diabetes insipidus treated at the University Hospital at Ann Arbor, Mich. In 34 of these the etiologic factors were clinically or pathologically determined. Diabetes insipidus is a symptom complex produced by injury to the supraopticohypophysial tract and not a specific etiologic entity. In any case of diabetes insipidus thorough and repeated examination should be made to determine the etiologic factors. Urine concentration tests indicate that patients with diabetes insipidus receiving a limited intake of fluid continue to secrete urine of low specific gravity, with resultant loss of body weight. Such a response indicates organic damage along the supraopticohypophysial tract. Therapy should be directed toward the etiologic factor. Thus in some cases of neoplasm of the hypothalamus and pituitary and of Hand-Schüller-Christian disease a good response to roentgen irradiation is obtained, and antisyphilitic therapy corrects the diabetes insipidus resulting from syphilis. As diabetes insipidus is not infrequently the first symptom in cases of neoplasm, occurring eight months and six years before other evidence of the malignant growth in 2 of the cases reported here, roentgen irradiation of the hypothalamicohypophysial region may be worth while when the cause of the diabetes is undetermined. Of the various methods of administration of posterior pituitary as replacement therapy in the absence of the antidiuretic principle, intramuscular injection of pitressin tannate in oil seems the most desirable. Intranasal application of pitressin in jelly was the least satisfactory. Use of a low salt diet as an adjunct to other therapy may be worth a trial. Thyroidectomy should not be performed for diabetes insipidus unless there are other specific indications for the procedure.

Vasodepressor and Carotid Sinus Syncope.—Engel and his co-workers report the clinical, electroencephalographic, electrocardiographic and circulatory responses observed during a variety of syncopal reactions, including syncope provoked by venipuncture, by distention of the duodenum, colon, rectum or vagina, by hyperventilation and by carotid sinus reflex. Eighteen patients and volunteer subjects were studied. In some instances syncope was a chance occurrence in the course of an unrelated experiment. In other instances the clinical history suggested that a certain procedure such as distention of viscera or massage of the carotid sinus would provoke syncope. Vasodepressor syncope was provoked in 9 patients by venipuncture, by distention of the rectum, colon, duodenum or vagina, by hyperventilation or by stimulation of the carotid sinus. In addition, 6 cases of the cardioinhibitory type of carotid sinus syncope and 3 cases of the cerebral type were studied. Complete unconsciousness, characterized by unawareness, muscular relaxation and falling, was always accompanied by high voltage slow waves in the electroencephalogram, regardless of the mechanism by which unconsciousness was provoked. Lesser changes in consciousness, such as lightheadedness, giddiness and transient unconsciousness, were associated with less obvious slowing of the electroencephalogram, loss of alpha activity or no change at all. In 2 cases of the cerebral type of carotid sinus syncope the development of contralateral focal neurologic signs and symptoms without loss of consciousness was associated with abnormal waves from the ipsilateral cortex. Vasodepressor syncope could be provoked by a wide variety of sensory stimuli, but the significance of the stimulus to the subject seemed to be more important than the specific modality involved. Most of the symptoms of vasodepressor syncope were associated with falling arterial blood pressure, and unconsciousness did not develop until blood pressure had fallen to a low level. Symptoms could be relieved by returning the subject to the recumbent position, but they often recurred if the subject stood up again, even if the original stimulus had been withdrawn. The derangement in circulatory dynamics was apparently compensated for but not corrected by assumption of the recumbent position, presumably by avoiding the pooling effects of gravity. Recovery of consciousness may occur in the erect position; convulsive movements and increase in muscle tone seemed to aid recovery, but they were not essential. The value of having the patient exercise before standing up was evident.

Archives of Ophthalmology, Chicago

32: 89-166 (Aug.) 1944

Chronic Keratoconjunctivitis Associated with Nocardia. W. L. Benedict and H. A. Iverson.—p. 89.
Sarcoidosis with Retinal Involvement: Report of 2 Cases. S. Goldberg and F. W. Newell.—p. 93.
White Rings of Cornea: Report of Microscopic Examination. M. W. Jacoby and R. Dominguez.—p. 97.
Intranasal Drainage for Cure of Chronic Infection of Tear Sac: Initial, Transcanalicular, Inverted U Shaped Incision to Facilitate Full Opening of Tear Sac. D. J. Morgenstern.—p. 101.
Buccal Mucous Membrane Grafts in Treatment of Burns of Eye. R. Siegel.—p. 104.
Treatment of Metastatic Meningococcic Endophthalmitis: Report of Case. A. C. Krause and W. Rosenberg.—p. 109.
Strabismus in Adults: Analysis of Operative Results in 65 Cases. I. I. Shure.—p. 113.
Bilateral Teratoid Tumor of Limbus. E. Rosen.—p. 120.
Intrinsic Variability of Astigmatic Errors. J. I. Pascal.—p. 123.
Foster Kennedy Syndrome with Fusiform Aneurysm of Internal Carotid Arteries. I. S. Tassman.—p. 125.
Pathogenesis of Acute Glaucoma. L. Hess.—p. 128.

Bull. of the U. S. Army Med. Dept., Washington, D. C.

80: 1-122 (Sept.) 1944

*March Fracture: Report of 313 Cases. C. W. Hullinger and W. L. Tyler.—p. 72.
*Colorado Tick Fever: Report of 39 Cases. J. D. Collins.—p. 81.
*Meningococcemia. L. Ochs Jr., T. Weiss and M. Peters.—p. 86.
False Positive Serologic Reactions for Syphilis: Report of 100 Cases Following Routine Immunizations and Upper Respiratory Infections. A. B. Loveman.—p. 95.
Postoperative Problems Following Perforation of Colon. B. P. Colcock.—p. 106.
Method for Instructing Medical Technicians. D. E. Casad, T. A. Broderick and H. T. Haver.—p. 109.
Treatment of Mentally Disturbed Soldiers Overseas. M. Moore and P. D. MacLean.—p. 113.

March Fracture.—Hullinger and Tyler observed at Camp Wheeler 300 patients with 313 march fractures. Each patient showed either a fracture line or callus formation by x-ray examination. An additional large number of patients were seen who had many of the earlier signs of march fracture but never positive x-ray signs. There were about 450 patients in this group. The incidence of march fractures at this camp greatly increased beginning in March 1942, as a result of a training order issued in February, which stated that all trainees would carry rifles and full packs at all times during the training program, that the men would march by foot from one area to another instead of riding, and that they would move to adjacent areas frequently on the double time. This increased the admission to the hospital for march fractures to a peak of 66 for the month of May. On May 24 a memorandum was issued lessening the strenuousness of the training program, with the result that the number of cases fell off in June to 44 and in July to 17. While this type of fracture has been reported as occurring in the tibia, fibula, femur, calcaneus, pelvis and cuneiform, it is most frequently found in the second and third metatarsal bones. Prior civilian occupation may be a mild contributory factor in causing early fatigue. The weight of patients and their age do not seem to be contributory. The mechanism of fracture and healing would seem to be as follows: Because of the repeated minimal trauma, there is an incomplete fracture of a few of the bony trabeculations of the shaft, which is most often not visible on x-ray examination. This is followed by hemorrhage, which, being on the surface, produces an elevation of the periosteum. New bone is formed in the hematoma. Calcium deposits are seen in this area at an early date. If the trauma continues there is fracture of additional bone trabeculations and additional hemorrhage, further elevating the periosteum and giving rise to additional osteogenesis. There is then slight absorption of calcium at the fracture ends with the dehiscence becoming visible by x-ray examination. If the trauma ceases, the fracture proceeds to orderly healing with complete repair. Treatment should be complete immobilization to prevent motion at the fracture site. Complications are very few in cases treated by complete immobilization.

Colorado Tick Fever.—Collins states that cases of Colorado tick fever were encountered in May and June 1943 at Camp Carson Station Hospital. Thirty-nine men became ill with fever, chills, headache and myalgia lasting from one to two days, followed two days later by a relapse of similar character. A leukopenia was an almost constant finding. All of the men had sojourned in tick country, and the majority gave a history of being bitten by ticks. All were between the ages of 20 and 40, in supposedly good health until the present illness. In every instance a history was obtained of having bivouacked for several days in the vicinity of Lake George, near Colorado Springs, a region notorious for the number of ticks found there. All ticks removed in the hospital from these patients were identified as Dermacentor andersoni. Therapy was symptomatic, although sulfonamide drugs were used in 6 cases without noticeable benefit. Salicylates and codeine relieved the myalgia and headache to a large extent, and dehydration was combated by copious fluid, given intravenously when necessary. Laboratory facilities to investigate the cause further were lacking. Attempts to reproduce the disease in laboratory animals by others have been unsuccessful and the etiologic agent is as yet unknown.

Meningococcemia.—Ochs and his associates report that 6 cases of chronic meningococcemia without accompanying meningitis were recognized from a station hospital in this country during and following an outbreak of meningococcic meningitis. Chronic meningococcemia is characterized by irregular fever, arthralgias, myalgias and a skin eruption, the most characteristic lesion being a rose colored macule with a vesicular, pustular or petechial center of pinhead size. The diagnosis of meningococcemia can be suspected on clinical findings, but to the laboratory falls the responsibility of demonstrating the causative agent. Blood cultures for growing meningococci are more often positive if the blood is drawn when the temperature is rising or at its peak. Attempts to isolate organisms from the skin lesions were unsuccessful. Acute fulminating meningococcemia with or without meningitis is another form of meningococcic infection. Nine cases of this form have appeared at the authors' hospital during 1942, 1943 and 1944. One patient died suddenly before the disease was recognized, and 1 patient died suddenly twelve hours after treatment from pulmonary edema. The disease is so fulminating that one cannot wait for a confirmatory blood culture before instituting treatment. At present any patient showing a diffuse petechial, purpuric or macular rash, early coma or manifest restlessness with a leukocytosis is considered to have fulminating meningococcic septicemia. The blood culture is usually positive for meningococci. In 4 patients the diagnosis was immediately confirmed by demonstrating gram negative diplococci in a film of tissue juice obtained by cutting into a petechia. The authors were unable to determine the presence of hemorrhage into the adrenal glands. Although the clinical course of this disease is similar to the Waterhouse-Friderichsen syndrome, the authors have not diagnosed their cases as such. The histories of 3 patients with acute fulminating meningococcemia are described. The treatment of the fulminating cases is with one-sixth molar sodium lactate solution in isotonic solution of sodium chloride; sodium sulfadiazine intravenously and intramuscularly; adrenal cortex extract intravenously and intramuscularly; meningococcus antitoxin intravenously; 5 per cent glucose and saline solution intravenously; sodium citrate given with sulfadiazine orally; oxygen; recording of blood pressure, pulse, pulmonary signs for pulmonary edema and urinary output every two or three hours.

Indiana State Medical Assn. Journal, Indianapolis

37: 427-554 (Sept.) 1944

Study of Upper Respiratory Infections. F. E. Ball and C. D. Berry.—p. 427.
Combat Flight Surgeon in England. O. C. Olson.—p. 430.
Venereal Disease and Flying Personnel. R. Dyar and J. R. Scholtz.—p. 435.
Effect of Diet on Gastrointestinal Symptoms at Altitude. J. H. Tillisch.—p. 439.
Reactions of Nasopharynx to Heat, Cold and Disease, with Some Therapeutic Considerations. P. S. Mountjoy.—p. 443.
*Sulfadiazine Prophylaxis of Acute Infectious Diseases. H. A. Warren.—p. 447.
Low Back Pain. J. V. Luck.—p. 452.

Sulfadiazine Prophylaxis of Acute Infectious Diseases.—Warren reports experiences in the use of sulfadiazine in controlling both sick call and hospital admissions from acute infectious diseases in more than 9,000 men at the Army Air Forces Technical Training School, Truax Field, Madison, Wis. This study was conducted as a part of the Army Air Forces Rheumatic Fever Control Program. Sulfadiazine in a prophylactic dosage of 3 Gm. once weekly proved ineffective in reducing the incidence of acute infectious disease among a group of 140 soldiers, but in prophylactic doses of 1 Gm. daily it effectively reduced the incidence of certain acute infectious diseases among 9,000 soldiers. This effect was evident both on admissions to the outpatient department and on hospital admissions for acute infectious diseases. Diseases caused by beta hemolytic streptococci, scarlet fever and nasopharyngitis due to streptococci were most effectively influenced. A definite effect was also apparent on the incidence of rheumatic fever occurring at a later period than the effect on acute hemolytic streptococcus disease. There was no effect on diseases caused by virus infection or of unknown etiology under this method of prophylaxis. Among 9,000 men, only 34 toxic reactions were encountered, and none of them were serious.

Journal Industrial Hygiene & Toxicology, Baltimore

26: 211-254 (Sept.) 1944

Aluminum Therapy in Silicosis: Experimental Study. Donald E. Cummings Memorial Lecture, St. Louis, May 11, 1944. L. U. Gardner, M. Dworski and A. B. Delahant.—p. 211.
Determination of Barium in Atmospheric Dusts. H. Yagoda.—p. 224.
*Cadmium Poisoning in Industry: Report of 5 Cases, Including One Death. L. W. Spolyar, J. F. Keppler and H. G. Porter.—p. 232.
Absolute Efficiency of Impinger and of Electrostatic Precipitator in Sampling of Air Containing Metallic Lead Fume. R. G. Keenan and L. T. Fairhall.—p. 241.
Liver Injury in Dogs Exposed to Trichloroethylene. J. Seifter.—p. 250.

Cadmium Poisoning.—According to Spolyar and his associates cadmium poisoning in industry occurs from the accidental absorption of fumes or dust by way of the respiratory tract, seldom by ingestion. A symptom complex develops that is primarily referable to the respiratory tract and is manifested within four to eight hours by irritation of the nasopharynx, cough, headache and a metallic taste in the mouth. This is followed by a latent period of twenty to thirty-six hours, when the chief complaints are dyspnea and severe pain in the chest. Gastrointestinal complaints may develop, depending on the amount of cadmium swallowed. Cadmium poisoning by ingestion is usually manifested by symptoms referable to the gastrointestinal tract, namely persistent vomiting for a period of four to six hours with or without diarrhea. Cadmium, being a powerful emetic, seldom produces death when taken orally. This dual symptom complex may explain the scarcity of reported cases of cadmium poisoning occurring as a result of inhaling cadmium fumes or dusts, in that the gastrointestinal symptoms may have been looked for and were missing. The authors report the histories of 5 men who worked in a shop for flanging steel inlet pipes. Flanging was accomplished by a team consisting of two men, one known as the heater and the other as the flanger. The heater heated one end of the 6 inch pipe by means of a propane-oxygen blowtorch until it was cherry red. The flanger created a flange, or bevel, on the heated end of the pipe. This work had been done for six months, when a different type of pipe was supplied. Soon after beginning work, the men noticed more smoke than usual and a dense yellowish brown fume being emitted from the pipe. After all the 5 men who had worked on these pipes for about four hours each had become ill, the operation was discontinued. Death of 1 of these men, who had been longer exposed to the cadmium fumes, led to inquiry by the insurance company, which disclosed that the pipe was coated with cadmium. The authors present data on 38 additional cases of cadmium poisoning by inhalation. Of the total of 43 cases 6 were fatal, indicating a mortality rate of 14 per cent. Death occurs between the fifth and seventh day after exposure. Recovery occurs within seven to eleven days.

Journal of International College of Surgeons, Chicago

7: 257-336 (July-Aug.) 1944

Blast. H. Bailey.—p. 257.
Administrative Procedures in Handling of Discharge of Disabled Service Men. L. Sanders.—p. 263.
Classification of War Wounds. B. Hughes.—p. 275.
*Use of Plasma Whole Blood and Human Serum Albumin by Armed Forces. D. B. Kendrick Jr.—p. 289.
Gas Casualties. A. H. Waitt.—p. 296.
Anesthesia During Circumstances of War. E. A. Rovenstine.—p. 301.
Total Rupture of Posterior and Inferior Aspects of Bladder: Rectovaginal Fistula. A. J. Pavlovsky.—p. 308.
*Free Muscle Transplantation in Restoration of Lips and Cheeks. A. Prudente.—p. 312.

Plasma, Whole Blood and Human Serum Albumin.—Kendrick states that recent developments in the field of replacement fluids have not removed the necessity for whole blood transfusions. Whereas plasma and albumin are effective therapeutic agents in shock and burns, whole blood is still indicated in severe hemorrhage, secondary anemia from burns, infections, carbon monoxide poisoning and many medical diseases. Fresh whole blood and stored blood are used. In order to make fresh blood available in the "theater of operations," the distilled water bottle from the Standard Army-Navy Plasma Package will be salvaged and utilized. It may be necessary to have stored whole blood on hand for immediate use. Equipment will be provided in large fixed medical installations where whole blood can be collected under a "closed system" and stored in refrigerated boxes for a period of five to seven days. It is expected that most of the blood collected for storage will be taken from proved group O donors, thus making it possible to inject this blood into recipients of all types.

Free Muscle Transplantation.—Prudente's method consists in the transplantation of a piece of muscle completely separated from its muscular body and transported through a skin tube. The sternocleidomastoid and pectoralis major are the muscles of choice for the face. This operation has been used in 4 cases. Three cases involved defects of the angle of the mouth and the cheek, 1 resulting from noma and 2 from cancer. The fourth was a case of cancer of the floor of the mouth involving the jaw and the inferior lip. Two cases of the first group have already been reconstructed both anatomically and functionally. The other 2 are in the last stages of restoration. The author stresses the following points: 1. Healing of the muscular skin flap is always by first intention, because the union is made between tissues of the same nature. 2. After the first stage, when the muscle strip is isolated before its transplantation, it is transformed into a fibrous tissue, but after that transplantation, when it lies close to the healthy muscles of the new region, it recovers its normal aspect, corresponding to a true rehabilitation of the tissue. 3. After a few months the grafted muscle recovers its function, probably as the result of nervous penetration from neighboring muscles, and the patient is able to perform every movement. Whistling and spitting are possible with real contraction of the grafted muscle. 4. Microscopic examination of the grafted muscle shows that its structure is perfectly normal.

Journal-Lancet, Minneapolis

64: 253-290 (Aug.) 1944

Suggested Therapeutic Procedure for Treatment of Empyema by Closed Method: Preliminary Report. E. E. Carpenter.—p. 278.
Counterirritation. A. C. Moorhead.—p. 280.

64: 291-324 (Sept.) 1944

Address of the President. J. C. Ohlmacher.—p. 302.
Address of President-Elect. D. S. Baughman.—p. 310.
Students' Health Service Experience in Outpatient Care of Army Students. M. M. Weaver and R. G. Hinckley.—p. 311.
Differential Diagnosis of Acute Glaucoma. F. N. Knapp.—p. 315.

Journal of Neurosurgery, Springfield, Ill.

1: 299-364 (Sept.) 1944

Basilar Impression (Platybasia) Case Secondary to Advanced Paget's Disease with Severe Neurologic Manifestations: Successful Surgical Result. H. T. Wycis.—p. 299.
Histologic Studies of Brain Following Head Trauma: IV. Late Changes; Atrophic Sclerosis of White Matter. J. P. Evans and I. M. Scheinker.—p. 306.
Extradural Cerebellar Hematoma: Case Report. F. Turnbull.—p. 321.
Bilateral Nerve Deafness, Persistent Cough and Paroxysmal Hyperpnea Due to Tumor in Floor of Fourth Ventricle. D. Weller.—p. 325.
Tantalum Cranial Clip. W. B. Hamby.—p. 331.
*Operative Results in Intervertebral Disks. F. C. Grant.—p. 332.

Operative Results in Intervertebral Disks.—Grant reviews observations on 150 patients with ruptured intervertebral disks verified at operation. All of these patients had at least a six months follow-up period. Before operation 11 patients were bedridden, 27 were unable to do gainful work and 112 were working with disabilities. Of the 11 bedridden patients, 6 are back at their previous jobs, 3 are employed in less arduous labor and 2 are unable to work. Among the 27 unable to work preoperatively 17 are back at work, 6 are improved and 4 are unimproved. Of the 112 patients working with disability, 55 are cured, 47 are improved and 10 not improved following surgical intervention. The author also reviews the results of conservative treatment of 93 patients with an assured diagnosis of ruptured disk. Of 15 bedridden patients 9 have completely recovered and 3 have improved enough to carry on light work. Of 42 who were unable to work, 36 have recovered sufficiently to return to less arduous work; the other 6 are still not working. Thirty-six who were working with disabilities are still at work, although 24 of them have had to change their employment. On the basis of this assessment the author sees no reason to change the conservative attitude he has adopted in the past two years. Surgery is not, in his opinion,

the only treatment for this condition. Many of these patients will recover with rest, leg traction, back support and other nonoperative means. If this is unsuccessful, or if a recurrence of pain is noted, surgery should be considered.

Michigan State Medical Society Journal, Lansing

43: 625-720 (Aug.) 1944

War Casualties in General Hospital in U. S. A. R. H. Kennedy.—p. 657.
Malaria: Current and Postwar Medical Problem. L. T. Coggeshall. —p. 662.
Intussusception. L. J. Gariepy and R. M. Atchison.—p. 665.
Peculiarities in Physiology of Newborn Patients. C. A. Smith.—p. 668.
Poliomyelitis: Contrast Between Kenny and Orthodox Concepts with Results of Treatment. Elizabeth Kenny.—p. 673.

43: 721-840 (Sept.) 1944

Health Needs of Nation as Reflected by Selective Service. L. G. Rowntree.—p. 769.
Neglected Interns. L. R. Leader.—p. 777.
Analysis of Deaths Occurring in Michigan from Pneumonia (All Forms). A. B. Mitchell.—p. 779.

New England Journal of Medicine, Boston

231:279-314 (Aug. 24) 1944

*Pain and Disability of Shoulder and Arm Due to Herniation of Nucleus Pulposus of Cervical Intervertebral Disks. J. J. Michelsen and W. J. Mixter.—p. 279.
Serologic Types of Hemolytic Streptococci Isolated from Scarlet Fever in Massachusetts, 1942-1943. S. M. Wheeler and G. E. Foley.—p. 287.
Polyarthritis in Sickle Cell Anemia. H. G. Brugsch and Dorothy Gill. —p. 291.
Recent Advances in Surgery (concluded). A. Blalock.—p. 293.

Disability of Shoulder and Arm Due to Herniation of Nucleus Pulposus.—Michelsen and Mixter report observations on 8 cases of herniation of the nucleus pulposus in the lower cervical spine. There were lesions at the fifth cervical interspace in 4 cases, at the sixth in 3 and at the seventh in 1, with involvement of the sixth, seventh and eighth cervical roots, respectively. The clinical data were brought together in a syndrome that comprised root pain and local sensory and motor disturbances, as well as positive x-ray, cerebrospinal fluid and iodized oil findings. The distribution of the sensory abnormalities was compared with standard dermatome charts. In these cases the sixth cervical dermatome seemed to involve the scapula, the anterolateral aspect of the upper arm, the antecubital space, the radial forearm and its thumb and index finger. The seventh cervical dermatome seemed to involve the scapula, the posterolateral aspect of the upper arm and the dorsal surface of the forearm and the index and middle fingers. The eighth cervical dermatome seemed to involve the scapula, the inner and upper arm, the forearm and the little finger. The importance of a systematic neurologic examination in cases of pain or disability of shoulder and arm is emphasized in order to separate the apparently specific syndrome of cervical herniations of the nucleus pulposus from other extraspinal and intraspinal entities. All of the 8 reviewed cases were proved by operation. All the patients had various forms of treatment prior to their hospital admission, without permanent relief. Such measures comprised baking and massage, lamp treatments, strappings and head traction. One patient was injected locally with procaine hydrochloride. The laminectomy and removal of the disk fragment produced good results in 6 cases. In 1 case the improvement was not too impressive. In 1 case in which the disk fragment could not be removed for technical reasons the pain was relieved but the motor disability persisted.

231: 315-342 (Aug. 31) 1944

*Chronic Latent Hepatitis Following Catarrhal Jaundice. M. D. Altschule and D. R. Gilligan.—p. 315.
Dislocation of Knee Joint: Report of 2 Cases. J. W. Sever.—p. 318.
Boston Medical Library. D. Cheever.—p. 320.
Late Effects of Total and Subtotal Gastrectomy. F. J. Ingelfinger.—p. 321.
New Hampshire Medical Society: Proceedings of the One Hundred and Fifty-Third Anniversary, House of Delegates, May 15 and 16, 1944. —p. 327.

Chronic Latent Hepatitis Following Catarrhal Jaundice.—Altschule and Gilligan state that there are now available in the literature records of the persistence of icterus as well as reports describing increased plasma bilirubin and decreased bilirubin excretory function in some patients who years previously had had an attack of catarrhal jaundice. Chronic gastrointestinal complaints and chronic hepatic enlargement have also been reported as sequelae of acute catarrhal jaundice. The present report of laboratory and clinical studies made in an unselected series of 36 persons who had had catarrhal jaundice one to twenty-nine years previously similarly demonstrates in some cases the persistence for years of certain evidences of hepatic dysfunction. Hyperbilirubinemia was detected in 9 of the 36 patients. It is probable that the incidence of impairment of liver function was even higher, since the distribution of plasma bilirubin values revealed an abnormally large number in the high normal range. Nine subjects in the entire group had palpable livers and 1 a palpable spleen. The chronic latent liver disorder revealed by this study was not accompanied by symptoms and did not appear to be progressive. It is concluded that a mild, benign form of chronic hepatitis is frequent after catarrhal jaundice.

North Carolina Medical Journal, Winston-Salem

5: 265-312 (July) 1944

Psychiatry Today. K. E. Appel.—p. 265.
Treatment of Kidney Disease and Hypertensive Vascular Disease with Rice Diet: II. W. Kempner.—p. 273.
Changing Phases in Treatment of Tuberculosis. P. H. Ringer.—p. 274.
Child Guidance: Responsibility of Every Physician. M. J. Carson. —p. 277.
The 1915 Serbian Typhus Epidemic. W. C. Davison.—p. 282.
Diagnosis of Eye Conditions Frequently Seen in General Practice. G. B. Sharbaugh.—p. 285.

5: 313-412 (Aug.) 1944

President's Message: Some Further Considerations Relative to Extension of Medical Care in North Carolina. P. F. Whitaker.—p. 313.
Benjamin Waterhouse (1754-1846) and Introduction of Vaccination into America. J. C. Trent.—p. 317.

Review of Gastroenterology, New York

11:223-290 (July-Aug.) 1944

Chronic Gastritis. F. Cunha.—p. 239.
Gastrointestinal Symptoms in Relation to Hypertension and Renal Disease. B. Jablons.—p. 246.
Management of Ulcer Syndrome. B. M. Bernstein.—p. 254.
Celiac Syndrome. B. Kramer.—p. 256.
Inflammable Physiologic Gases in Rectum and Colon, with Report of Case. W. Lieberman.—p. 259.

Western J. Surg., Obst. & Gynecology, Portland, Ore.

52: 359-406 (Sept.) 1944

Protection for Industrial Women: Progress and Prospects. Mary Anderson.—p. 359.
Why Do Women Stay Away from Work? Preliminary Report. C. O. Sappington.—p. 363.
Practical Industrial Health for Women. F. B. Wishard.—p. 368.
Report of Committee on Health of Women in Industry: Section on Obstetrics and Gynecology of American Medical Association. H. C. Hesseltine and others.—p. 372.
*Use of Methergine (Synthetic Ergonovine) in Third Stage of Labor: Preliminary Report. P. C. Roberts.—p. 380.
Methergine (Synthetic Lysergic Acid Derivative) a New Oxytocic: Preliminary Report. D. G. Tollefson.—p. 383.
Treatment of Chronic Arthritis. J. A. Key.—p. 385.

Methergine (Synthetic Ergonovine) in Third Stage of Labor.—Roberts reports observations on a new synthetic ergonovine which is known as methergine. This substance, which was synthesized by Stoll and Hofmann of Basel, Switzerland, is particularly important because of the potential shortage of rich ergot of rye. Methergine was first employed subcutaneously in 26 cases which were observed in the Department of Obstetrics of Stanford University Hospital. No systemic reactions were encountered in any of these cases. Methergine was then administered intravenously in the third stage, in doses of 1 cc. containing 0.2 mg., to 34 patients, of whom 6 were primiparas and 28 multiparas. The contraction of the fundus following methergine was stronger and of considerably greater intensity and duration than with the usual ergonovine preparations. No increase in the incidence of postpartum morbidity or subinvolution of the uterus was noted in this series. Experience with methergine has convinced the author that it is a useful, potent oxytocic of great value. Of particular interest has been the reduction of blood loss in the third stage of labor—not necessarily the lowering of the level within normal limits, but rather the elimination of those cases of severe hemorrhage of over 500 cc. In view of the small series, the results with methergine require further verification.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Experimental Pathology, London

25: 27-80 (April) 1944. **Partial Index**

Observations on Bactericidal and Bacteriostatic Actions of P.-Aminobenzenesulfonamide and P.-Hydroxylaminobenzenesulfonamide, with Special Reference to Their Suppression by P.-Aminobenzoic Acid. J. W. McLeod, Anna Mayr-Harting and N. Walker.—p. 27.

Effect of Cell Growth Promoting Tissue Extracts on Healing of Experimental Cutaneous Wounds in Rats: I. Local Application. E. Auerbach and L. Doljanski.—p. 38.

Effects of South Wales Anthracite Coal and of Precipitated Amorphous Silica on Lungs of Mice. J. A. Campbell.—p. 46.

Experiments on Inhibitor Occurring in Rous No. 1 Sarcomas. J. G. Carr.—p. 56.

Action of Sulfonamides Against Treponema Recurrentis. F. Hawking.—p. 63.

British Medical Journal, London

2: 169-200 (Aug. 5) 1944

Penicillin: Survey. H. W. Florey.—p. 169.

*Treatment of Acute Empyema with Penicillin. E. C. B. Butler, K. M. A. Perry and F. C. O. Valentine.—p. 171.

Penicillin in Ophthalmology. J. G. Milner.—p. 175.

Penicillin and Sulfonamides in Infantile Gastroenteritis. Elizabeth Burns and W. Gunn.—p. 178.

Severe Hemolytic Transfusion Reaction Due to Rh Factor. A. Beck, C. V. Harrison and J. M. Owen.—p. 180.

Penicillin in Treatment of Acute Empyema.—Butler and his associates dissolved penicillin in water to give a concentration of 1,000 units per cubic centimeter, and the dosage was adjusted to the size of the cavity. The sensitivity of the infecting organism having been established, the initial injection varied between 10,000 and 40,000 units, 20,000 being usual. As treatment proceeded, 10,000 or 5,000 units often sufficed. The authors treated 18 cases. Seventeen of these were infected. In 10 the invading organism was the streptococcus and in 7 the pneumococcus. In 1 patient with sterile traumatic hemothorax, treatment with penicillin prevented infection. The infected cases treated with penicillin show that, provided the infecting organism is susceptible, an empyema cavity can be sterilized by repeated aspiration of the pus and injection of penicillin and the toxic condition is thereby relieved. It is too early to assess the final results of the treatment, since further improvement is expected in some cases, while symptoms may yet develop in others arising from pulmonary fibrosis. The period required for final sterilization is unpredictable, since some cases showed recurrence after eight to ten days of continuous treatment, whereas some remained sterile after only five days' treatment. After sterilization there was the tendency for sterile pus to be formed in which minute gram positive cocci persisted. It seems possible that these organisms, although dead, may remain pyogenic. The source of these organisms and of normal cocci in cases of recurrence is probably to be found in the masses of fibrinous exudate lining the walls of the cavity, the removal of which might be expected to hasten sterilization and limit the formation of pus. To accomplish the removal of this exudate some recommend irrigation of the cavity with sterile saline solution before injecting penicillin, while others advise rib resection and removal of the fibrinous masses lining the cavity as soon as the infection is under control and the patient fit for the operation. There is little hope of avoiding a thickened pleura and rigid chest wall without removal of the fibrinous masses.

2: 201-232 (Aug. 12) 1944

Nutritional Status of Cambridge School Children. J. Yudkin.—p. 201.

Nutrition and Scholastic Attainment. I. F. MacKenzie.—p. 205.

Koilonychia and Its Recovery in Cases of Thyrotoxicosis. Lorna Cooke and Stella M. Luty.—p. 207.

Histologic Effect of Injection of Mepacrine (Atabrine) Dihydrochloride. F. Hawking.—p. 209.

Sterilization of Skin by Colorless Flavine (5-Amino-Acridine). V. Bonney and H. S. Allen.—p. 210.

*Pituitary Cachexia Treated with Corticotropic Hormone. R. E. Hemphill and M. Reiss.—p. 211.

Pituitary Cachexia Treated with Corticotropic Hormone.—Hemphill and Reiss describe the case of a woman whose menses ceased abruptly at the age of 39 without subjective menopausal disturbances. She became depressed, lost appetite and imagined that her viscera were deranged and the bowels "stopped up"; she attempted suicide. She was thin, weak, and frail looking. The skin was extremely dry. The hair of the head was brittle and lusterless, that of the pubis and axillas scanty; muscle bulk was reduced. There was no assayable output of gonadotropic, corticotropic or thyrotropic hormones in the total urine of ninety-six hours; the output of 17-ketosteroids was only 2.6 mg. in twenty-four hours. Forty sudanophobic units of corticotropic units were administered daily for twenty-four days. There was immediate improvement. Two months later a further course of daily injections of 25 units was given for fourteen days. This treatment resulted in complete restoration of weight and cosmetic features. This was not a case of anorexia nervosa. The psychotic depression was not relieved until a considerable time after physical improvement was complete. It is now two years since hormone treatment has been given, but the improvement has been maintained.

Edinburgh Medical Journal

51: 209-256 (May) 1944

Controversy on Contagiousness versus Noncontagiousness of Leprosy, with Particular Reference to Dr. W. Munro's Contributions Published in Edinburgh Medical Journal. E. D. W. Greig.—p. 209.

Some Problems of Communal Feeding. C. P. Stewart.—p. 215.

Abdominal Pain in Pregnancy. E. C. Fahmy.—p. 229.

Biochemical Classification of Coliform Bacilli in Sputum. R. Salm.—p. 247.

51: 257-304 (June) 1944

War Wounds of Abdomen: Report of 64 Cases Treated by Laparotomy. A. G. R. Lowdon.—p. 257.

*Propylene Glycol Vapor as Air Disinfectant: I. S. W. Challinor and J. P. Duguid.—p. 280.

Experimental Cancer Research. J. F. Riley.—p. 290.

Propylene Glycol Vapor as Air Disinfectant.—Challinor and Duguid investigated the efficiency of propylene glycol vapor as an air disinfectant (*a*) in air continuously infected by atomization of suspensions of Bacillus prodigiosus and (*b*) in a crowded room with its natural, largely dust borne, air infection. The effect of single vaporizations of the glycol was found to be transient. Reduction of air infection could be maintained by continuous vaporization of the glycol or by single vaporizations repeated at short intervals of about ten minutes. Vaporization at the rate of 1 cc. of glycol per million cubic centimeters of air per hour produced a considerable reduction (about 85 per cent) in the naturally present air infection of a crowded room during the period of vaporization; perceptible mist formation, which might be found objectionable in practice, occurred at this dosage rate. Vaporization at lower rates did not result in mist formation but produced only small reductions in the air infection.

Lancet, London

2: 197-230 (Aug. 12) 1944

Major Complications of Penetrating Wounds of Chest. A. L. D'Abreu, J. W. Litchfield and C. J. Hodson.—p. 197.

Primary Tuberculous Infection in Nurses: Manifestations and Prognosis. M. Daniels.—p. 201.

Processing of Plasma with Kaolin. M. Maizels.—p. 205.

Crush Kidney Syndrome in Cat. M. Grace Eggleton.—p. 208.

*Treatment of Typhus with Anti-Typhus Horse Serum. M. Wolman.—p. 210.

Treatment of Typhus with Anti-Typhus Horse Serum.—According to Wolman typhus in Addis Ababa is louse borne. Epidemiologic, immunologic and clinical studies have shown that it is epidemic typhus, identical with the European disease. The mortality varies from year to year and from month to month. The observations reported in this paper extended over a period of eighteen months and covered two major epidemics. The patients were mostly Ethiopians. All patients admitted with symptoms of typhus were given a special chart with a serial number. Venous blood, taken on the day the provisional diagnosis was made, was sent to the Medical Services Laboratory for Weil-Felix and Weigl tests. Patients with even numbers were given symptomatic treatment only. Patients with uneven numbers were given the same symptomatic treatment, plus serum. The total number of patients was 440. For the

preparation of the serum the Ethiopian army lent 2 horses. Living rickettsias contained in the intestines of lice, prepared for Weigl vaccine, were injected into the horses, usually every five to six days, in doses increasing over a period of two and one-half months. The horses were then bled twice (five and ten days after the last injection). In each subsequent month a further series of injections was given (ordinarily 250, 375 and 500 louse intestines) followed by two further bleedings. The blood was collected in large sterile bottles one-tenth full of 5 per cent sodium citrate, and after two or three days the supernatant serum was siphoned off and enclosed in rubber capped bottles, with merthiolate or phenol as a preservative. The dosage of serum was 20 cc. subcutaneously twice on the first day and once on three succeeding days. The mortality of the treated group was 3.6 per cent, compared with 10.9 per cent in the controls. The serum seemed to shorten the illness and reduce the incidence of psychotic symptoms. Its influence was greater when given early in the illness.

Medical Journal of Australia, Sydney

2: 49-76 (July 15) 1944

*March Hemoglobinuria: Description of Features of This Condition and Report of Case. Lucy M. Bryce.—p. 49.
Some Observations on Tuberculosis Control. H. Roche.—p. 52.
Experiment on Complete Transformation of Scrotum into Marsupial Pouch in Trichosurus Vulpecula. A Bolliger.—p. 56.

2:77-100 (July 22) 1944

Sporadic Occurrence of Influenza in Victoria During 1943. W. I. B. Beveridge and S. E. Williams.—p. 77.
Modern Management of Prostatic Obstruction. R. J. Silverton.—p. 80.
Precipitin, Agglutination, Indole and Methyl Red Reaction of Dysentery Bacilli. F. Draper.—p. 84.

March Hemoglobinuria.—This is a condition in which physical exertion, usually in the form of marching, is followed by the passage of red or dark colored urine. The author lists the following salient features of march hemoglobinuria: 1. It occurs in young males, usually in the second or third decade. 2. It is related to exercise in the upright position. 3. Constitutional symptoms are absent or mild. 4. The course is benign. The condition appears to have no permanent ill effects, and it progresses without specific treatment toward ultimate spontaneous recovery, which usually takes place within a period of months or a year or two after the initial attack. Occasionally it is of longer duration. In 1 case periodic attacks occurred for seven years, and in another case attacks occurred intermittently for twenty years. The essential nature of the condition—that is, its relation to exercise in the upright position and the absence of associated physical abnormalities or after-effects, may tend to cause delay in diagnosis. This occurred in the case reported. A corporal who enlisted in the Australian Military Forces at the age of 18 noticed that his urine was "dark" after more than usually strenuous military training exercises, but as he felt otherwise quite well, and as the condition did not persist, he did not report this attack at the time. Several months later another attack occurred, associated this time with some pain in the groins. Eight hours later he reported at the hospital. No abnormalities were detected on physical examination. Three days after his return to camp another attack occurred in which the passage of "dark" urine was associated with pain in the right loin. He was admitted to the hospital, but again no abnormalities could be detected. At several successive hospitalizations numerous tests were made, and finally it was discovered that a march of forty-five minutes' duration was followed by hemoglobinuria. The author points out that the usual program of investigations designed to demonstrate or exclude the more common causes of hematuria or the presence of abnormal pigments in the urine is almost certain to be carried out with the patient at rest. By virtue of this fact a sojourn in a hospital for investigation will actually tend to prevent the occurrence of march hemoglobinuria and so fail to reveal the symptoms of which the patient complains. Unless, therefore, the possibility of march hemoglobinuria, which at least in its severe forms is rare, is kept in mind, considerable difficulty and delay may occur in confirming the patient's statements and establishing the diagnosis.

Revista Chilena de Pediatría, Santiago

15:249-323 (April) 1944. **Partial Index**

Medical and Social Problem of Asphyxia of the Newborn. E. Cienfuegos.—p. 249.
*Neurologic Complications of Typhoid. B. Bambach and P. Guerrero.—p. 278.
Trichinosis in Children. F. Martinez L. de G.—p. 297.
Pulmonary Atelectasis in Children and Its Relation to Primary Tuberculosis.—p. 316.

Neurologic Complications of Typhoid.—Bambach and Guerrero present the histories of 2 children with typhoid who had neuropsychic complications that masked the course of the typhoid. The first child, aged 5, had hemiparesis of the right side, which was probably of central origin. The process was most severe in the lower extremity, and since there was no involvement of the tongue it is assumed that the lesion was located in the upper part of the left rolandic convolution. The neurologic symptoms completely disappeared; a neurologic examination made fifty-eight days after hospitalization was negative. The diagnosis of typhoid was amply corroborated by a positive Widal reaction and a typical blood picture. The second case concerned a child aged 6 who was hospitalized with an undetermined infectious disease. The symptomatology indicated involvement of the nervous system, but the case remained undiagnosed for a long time. Finally blood culture yielded Eberth's bacillus, and a 1:100 positive Widal reaction was obtained. The authors reviewed 100 cases of typhoid that were observed at their hospital during recent years. Excepting cases with only dulling of the sensorium, there were 15 with neurologic signs. This contrasts with only 1.73 per cent of neurologic involvement in an epidemic in Lyon in 1928-1929 and with only 4 per cent reported from Uruguay. The authors think that this diversity of percentages speaks for differences in the type of epidemic or for regional peculiarities. In the cases reviewed by them the mortality of the cases with neurologic involvement was 23 per cent. The cases which do not have a fatal outcome are usually reversible and have no sequelae.

Münchener medizinische Wochenschrift, Munich

89:923-946 (Oct. 30) 1942. **Partial Index**

*Differential Diagnosis of Icterus Catarrhalis and of Hepatitis Epidemica: I. Varieties of So-Called Icterus Catarrhalis. R. Mancke and W. Siede.—p. 923.
Lead Poisoning from Drinking Water, Its Clinical Importance, Public Health Aspects and Prophylaxis. W. Kollath.—p. 927.
Etiology and New Causal Lipoid Therapy of Neuroses. R. Bleibrunner.—p. 931.
Problem of Combined Treatment with Strophanthin and Glucose. H. Lachmann.—p. 935.

Differential Diagnosis of Catarrhal Jaundice and of Epidemic Hepatitis.—Mancke and Siede report their observations in 456 cases of so-called icterus catarrhalis. Three groups are differentiated: 1. The specific icterus catarrhalis, which starts with intestinal symptoms, frequently without any rise of temperature. Alimentary or endogenous intestinal toxins may reach the liver cells by the portal vein or by the intestinal lymph radicles. It is characterized by its deleterious effect on the membrane. Toxic edema of the liver, serous hepatitis combined with destruction of liver cells, may be the result ("forme fruste" of the acute and subacute atrophy of the liver). 2. Capillary cholangitis, which may develop by ascending from the large bile ducts or which may be of hematogenous origin; in the latter case one may have to deal with a cholangitis of excretory type. The injurious agent is bacterial in the majority of these cases. A lesion in the area of the "intermediary portion" of the bile ducts may occur first. The bile ducts are lined with epithelium and are connected with the intercellular bile capillaries of the liver; "intermediary portion" is the term used for this first portion of the bile ducts. It deserves special morphologic consideration as a particularly vulnerable area of the bile ducts. An icterus of fine mechanical origin from obstruction in the area which contains the sources of bile may result from the lesions in the aforementioned area. 3. The specific hepatosis. Direct destruction of liver cells may be caused by a hematogenous toxin of liver cells whose chemical structure may be more or less ascertained. Arsphenamine, cinchophen, chloroform and phosphorus may be mentioned. Fatal hepatargy may result from toxic hepatosis induced by mushroom poisoning.

Book Notices

The Chemistry and Technology of Food and Food Products. Prepared by a Group of Specialists Under the Editorship of Morris B. Jacobs, Ph.D., Senior Chemist, Department of Health, City of New York. Volume I. Cloth. Price, $10.50; $19 per set of 2 volumes. Pp. 952, with 79 illustrations. New York: Interscience Publishers, Inc., 1944.

This is the first of two volumes devoted primarily to a complete description of the technical aspects of foods, their sources, composition, processing and also the related body physiology. Each chapter has been prepared by a specialist in the field; altogether forty-one individuals collaborated in the work, with the whole edited by one well versed in the broad subject of food control. Two of the six sections of this treatise on foods comprise volume I. The first deals with fundamental food chemistry and body processes related to foods. The chemical discussion of the basic food constituents is extensive and well done. The physiologic coverage is less complete, but this subject may be considered of secondary interest in this book. Use of the term "vitagen," referring to the so-called essential fractions of the basic food constituents, is of dubious value. The brief mention of disease conditions resulting from lack of food substances is incomplete. For example, iodized salt is not included as a food source of iodine, the preventive of simple goiter.

The second section of this volume presents widely diversified information on every basic type of processed and unprocessed foodstuff, as well as beverages and condiments. For each class a historical sketch is given followed by information on growth and production, varieties available, chemical composition, methods of preservation, government controls and standards of identity, as well as other facts of interest. The numerous tables offer valuable sources of reference data, although some of the data so supplied are not the most recently available and in some instances the vitamin values are given in units now considered obsolete. The presentation is strictly scientific throughout, with support of frequent references to the literature and inclusion of a bibliography at the end of each chapter. This volume is a combination of textbook on food chemistry and encyclopedia of basic food information. It represents an ambitious undertaking which has gathered together a great deal of information, heretofore unrelated, for the benefit of science and industry.

Lippincott's Quick Reference Book for Medicine and Surgery: A Clinical, Diagnostic and Therapeutic Digest of General Medicine, Surgery, and the Specialties, Compiled Systematically from Modern Literature. By George E. Rehberger, A.B., M.D. Twelfth edition. Fabrikoid. Price, $15. Pp. 1,460, with 305 illustrations. Philadelphia, London & Montreal: J. B. Lippincott Company, 1944.

In this edition the sections on gynecology and genitourinary diseases have been entirely rewritten, and the list of drugs has been revised in accordance with the new Pharmacopeia and National Formulary. The publisher points out that the advances in medicine have been so great that scarcely a page of the book has gone unchanged. Special attention is called, however, to new material on chemotherapy, shock treatment, burns, deficiency diseases and nutrition. Many new color plates have been added to the present edition of this well known encyclopedia.

Health Counseling for Girls. By Margaret L. Leonard, Ed.D. With a foreword by Ruth Strang, Ph.D. Cloth. Price, $1.50. Pp. 131. New York: A. S. Barnes & Company, 1944.

This is a valuable book for any one who has to interview girls in connection with physical education, health education or administrative work (advisers and deans) and for personnel directors in industries employing many women. The book is devoted to an exposition of technics. It starts with a chapter in which are summarized interviews with eight girls presenting different health and personal problems. These interviews are analyzed in terms of approach, interview technics, the use of records and suggested ways of asking questions. The author concludes that, allowing for emotional disturbance, shyness, suspicion and the like, adolescents, for the most part, appear to try sincerely to give honest answers to questions. The second chapter deals with health counseling as part of a total school program. This includes much valuable information as to the role of the counselor and how it can best be discharged. Chapter III deals with specific health counseling problems, such as loss of weight, absence due to abdominal pain and nausea, return to regular physical education after illness, dental care problems, deafness, health in relation to selecting a college and the lighter school program after a month's absence due to pneumonia, nail biting, cardiac patients and stair climbing, skin disorders and so on. Extreme overweight or underweight, menstrual problems, fatigue, posture, faulty elimination, personal fastidiousness, difficulties with school work, boy and girl relationships and getting along with other girls are other topics dealt with. Chapter IV deals with the interrelationship of counseling and group activities among adolescents. In these four brief chapters the topics are dealt with effectively, clearly and briefly but not dogmatically. This should be an excellent reference and handbook for the purposes suggested in its title.

The Blood Plasma Program. By James A. Phalen, M.D., Colonel, U. S. Army. Issued by the Office of Medical Information (Under Grant of the Johnson & Johnson Research Foundation). National Research Council, Division of Medical Sciences. Paper. Pp. 67. Washington, D. C., 1944.

Spontaneous Pneumothorax. By James J. Waring, M.D. Issued by the Office of Medical Information (Under Grant of the Johnson & Johnson Research Foundation). National Research Council, Division of Medical Sciences. Paper. Pp. 34, with 2 illustrations. Washington, D. C., 1944.

Antimalarial Drugs: General Outline. By Owsei Temkin, M.D., and Elizabeth M. Ramsey, M.D. Issued by the Office of Medical Information (Under Grants of the Carnegie Corporation and the Johnson & Johnson Research Foundation). National Research Council, Division of Medical Sciences. Paper. Pp. 128, with illustrations. Washington, D. C., 1944.

These three mimeographed pamphlets, all issued by the Office of Medical Information of the National Research Council, are brief informative monographs on timely subjects. Of the three under review, the one on "Antimalarial Drugs" is the most extensive, since it includes a bibliography of 237 titles. The publication of these brochures has been made possible by grants from the Johnson and Johnson Research Foundation, and in the case of the publication on "Antimalarial Drugs," with the help of the Carnegie Corporation as well. All three publications are useful and authoritative within the limits of the space employed.

Sex Education in Schools and Youth Organisations. Board of Education Educational Pamphlet No. 119. Paper. Price, 15 cents; 6d. Pp. 22. New York: British Information Services; London: His Majesty's Stationery Office, 1943.

In Britain, as in the United States, sex education is approached gingerly, with many misgivings, false starts, a furtive rather than forthright approach. Every one agrees that it should be done and every one gives a sigh of relief when some one else shows signs of doing it. Lectures, conferences, pamphlets and books have all been tried in Britain, as they have in the United States, and it all comes down to the fundamental question of who is doing the teaching. Given a teacher of appropriate personal qualifications, all goes well; lacking such a teacher, no system and no literature has any effectiveness or validity. In Britain, as in the United States, "it is the general view that sex instruction should be given as a related part of a wider course, especially biology, so that sex and reproduction may be introduced in their proper places without undue emphasis. Many schools, however, are without biology teaching and in others the biology staff are not anxious to give the instruction. In these cases special classes are often necessary." This could have been written with equal validity about the American situation, as could this: "Invariably parents are relieved to know that the question has been discussed but get foolishly hot and bothered if their wishes are consulted beforehand."

The Medical Annual: A Year Book of Treatment and Practitioner's Index. Sir Henry Tidy, K.B.E., M.A., M.D., and A. Rendle Short, M.D., B.S., B.Sc., Editors. Sixty-Second Year 1944. Cloth. Price, $7. Pp. 404, with illustrations. Baltimore: Williams & Wilkins Company, 1944.

This yearbook continues through the war years and constitutes essentially a collection of abstracts largely from British and American publications. There are occasional rare references to the literature of central Europe, and these are mostly in relation to subjects concerned in the war.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

ADOPTION FROM FAMILIES OF POOR STOCK

To the Editor:—**About two months ago I delivered a set of twins in the home. They weighed 6 and 6½ pounds (2,725 and 2,955 Gm.), and were the eighth and ninth babies of this mother. At about 1 month of age they were dehydrated and weighed about 4 pounds (1,815 Gm.) each, and since they were not well cared for by the mother they were entered in the hospital. The babies are back to normal now, and the mother wants some one to adopt them. One of my best friends has asked my advice about adopting them; how to answer him is my problem. The father of the children is in the penitentiary for stealing; the oldest son is in the county jail for the same offense. The mother is ignorant. The other children look and act well. The family is at the lowest economic level. What are the chances for these babies to inherit the traits of their father and brother?** **M.D., Alabama.**

ANSWER.—While the general opinion is that children do not inherit acquired characteristics, in selecting a child for adoption the average foster parent should feel that the stock of the baby is at least average in order that he may get an even break in setting the environment for the child he takes into his household. It would be decidedly questionable to adopt children with the type of family history given in this case. It is quite evident that they come from less than average stock. The only thing which would change this opinion would be some additional information about the ancestry of this family which might be more favorable.

FEVER OF UNKNOWN ORIGIN

To the Editor:—**A man aged 39 was admitted to the hospital because of nine days of remittent high fever of 105 to 99 F. daily, which did not respond to sulfonamides. The patient had had an occasional nonproductive cough and at the start of his illness had had a transient charleyhorse in his right leg, which had not annoyed him since. There were no other symptoms. The patient had not traveled outside of New York City, and there was no known contact with illness. The past history was entirely normal. On admission the patient appeared acutely ill and was shivering. Physical examination was entirely normal. The urine was normal. The blood count showed 11,000 white cells with 74 per cent polymorphonuclear cells, 4 per cent monocytes and 22 per cent lymphocytes. Of twelve blood cultures, nine were sterile and three showed Streptococcus viridans. On one occasion blood agglutinations showed typhoid positive 1: 80, paratyphoid A and B each positive 1: 160. A smear for malaria was negative. The temperature curve by days was 105, 98.6, 102, 98.6, 100 F. and normal thereafter. Spinal fluid examination was normal, as was an electrocardiogram and a chest plate. The stools showed no ova or parasites. What significance is attributable to the repeatedly positive culture for Streptococcus viridans in the absence of any other evidence for bacterial endocarditis? What type of treatment and follow-up are indicated? Can you suggest a diagnosis?** **M.D., New York.**

ANSWER.—Cases like the one described in which diagnosis cannot be made are not uncommon. It must be expected that not every case can be diagnosed. There are, no doubt, still some infections whose cause is unknown, and in other instances well known infections may occur without telltale evidence by which diagnosis may be made.

Data given in the case in question are incomplete. At what season of the year did it occur? What was the sedimentation rate of the erythrocytes? What was the nature of the "charley-horse"? Charleyhorse in Gould's Medical Dictionary is described as "a rupture or strain of muscle or tendon fibers generally resulting from athletic efforts." If the patient had this condition, the local injury and hemorrhage into the tissue, myositis, phlebitis or cellulitis may have served as the source of the trouble, which could begin with a chill, last nine days with remittent fever and not be influenced by sulfonamide therapy. On the other hand, the charleyhorse may have been mistaken for a small embolus, phlebitis or other condition.

The significance of Streptococcus viridans in the blood on several occasions is uncertain. This ubiquitous coccus may appear transiently and apparently harmlessly in the blood stream in many febrile diseases, and its presence has caused confusion in mistaking it for the cause rather than as a commensal. On the other hand, the attack described may be the first evidence of subacute bacterial endocarditis. If the patient remains well, no treatment is necessary. The patient should nevertheless be examined at intervals of several weeks for any abnormalities, especially for fever and evidence of cardiac valvular injury.

To suggest further diagnoses would be guesswork, but hidden, symptomless abscess (renal, perirenal, prostatic) may be mentioned.

PANCREATIC EXTRACTS FOR PERIPHERAL VASCULAR DISEASE AND ARTERIOSCLEROSIS

To the Editor:—**Of what use are pancreatic extracts in the treatment of peripheral vascular disease and arteriosclerosis? I am familiar with Dragstedt's experimental use of lipocaic in arteriosclerosis and have read the discussion of Wolffe's "Desympatone" The Journal, Oct. 26, 1940, (p. 1454), which is not very conclusive. Have there been any good clinical studies of the effect of a fat mobilizing pancreatic extract in these conditions? Is a reliable preparation of this sort available for clinical use?** **Elaine M. Thomas, M.D., Chicago.**

ANSWER.—There have been several clinical studies of the use of pancreatic tissue extract (insulin, histamine and choline free) in peripheral vascular disease. Whatever beneficial effects have been obtained with these extracts have been attributed by the users not to a fat mobilizing enzyme but to a vasodilating substance titrated according to its ability to neutralize the effects of epinephrine. It is understood that this vasodilating substance is not peculiar to pancreas but is found in several other tissue extracts.

Klein, Saland and Zurrow (Pancreatic Tissue Extract [Insulin Free] in the Treatment of Peripheral Vascular Disease, *Ann. Int. Med.* **18**:214 [Feb.] 1943) found that tissue extract injected intramuscularly in 3 cc. doses twice a week for relatively long periods (six to eighteen months) produced improvement in claudication time and rest pain but had no effect on existing tissue changes. They could not confirm the observations of Fisher, Duryea and Wright (Deproteinated Pancreatic Extract [Depropanex] *Am. Heart J.* **18**:425 [Oct.] 1939) that pancreatic tissue extract produced an immediate improvement in claudication time. Gorham and Climenko (The Role of Insulin Free, Histamine Free Pancreatic Tissue Extract in the Treatment of Peripheral Vascular Disease, *Am. Heart J.* **25**:486 [April] 1943), using the same type of pancreatic tissue extract, found it to have a beneficial symptomatic effect on nearly all patients with peripheral vascular disease when vasospasm was a prominent feature. In their series, patients obtained relief for periods of one to six months with administration at intervals of two to seven days. The pancreatic tissue extracts used in these studies included Depropanex (Sharp and Dohme), Tissue Extract No. 568 (Sharp and Dohme) and Pancreatic Hormone (Grant).

There have been no extensive clinical studies made of the effect of fat mobilizing pancreatic substances on arteriosclerosis and peripheral vascular diseases. Choline and lipocaic have thus far been studied chiefly in their effects on experimental animals. The standardization of lipocaic is difficult. Its use in a single case of xanthoma tuberosum (Rosenak, B. D.: *Ann. Int. Med.* **19**: 514 [Sept.] 1943) was reported to have been without effect on the lesions or plasma lipids. However, in following the implications of this question we presume to possess a greater knowledge of the pathogenesis and course of arteriosclerosis than is the case at present. It is not at all certain that arteriosclerosis is dependent primarily on a hyperlipemia, although Leary (*Arch. Path.* **32**:507 [Oct.] 1941) has offered an interesting series of demonstrations to show that cholesterol esters are deposited in the subendothelium of the aorta by wandering tissue cells and the arteriosclerotic process thus initiated. Others believe that the accumulation of lipids in an artery is secondary to medial injury. Furthermore, Leary differentiates between atheroma formation in the subendothelium, which he states is a reversible process, and atherosclerosis, which is a permanent chronic process due to prolonged stay of cholesterol esters in the intima. He believes the latter responsible for most of the important lesions listed under arteriosclerosis. The ability to remove atheromas, according to Leary, is chiefly a cellular function, being performed by fixed cells, "lipolytic fibroblasts," and this ability disappears gradually with age and other factors. However, even if it is assumed that these demonstrations open an avenue of therapy, it is difficult to see how proper clinical evaluation of any chemical agent can be made on the basis of its ability to mobilize fat from the blood vessels, since atherosclerotic changes cannot be detected by x-ray examination and most workers agree that there is no fixed relationship between blood lipid levels and arteriosclerosis.

ACETARSONE FOR SYPHILIS

To the Editor:—**What is the consensus concerning the use of acetarsone (stovarsol) in the treatment of prenatal syphilis? I am particularly interested in the results of experiments in the use of acetarsone and the treatment of syphilis in adults whose veins are so small as to make intravenous treatment impossible.** **Cecil A. Z. Sharp, M.D., Joliet, Ill.**

ANSWER.—Acetarsone is not suitable for the treatment of syphilis in adults, whether orally or by any parenteral route. The drug produces a high incidence of serious toxic reactions and cannot be recommended.

SHOCKLIKE STATE AFTER PNEUMONIA

To the Editor:—A man with an extensive right lower lobe pneumonia, probably pneumococcic, did not respond to sulfadiazine therapy in forty-eight hours and was given penicillin. On the fifth day of his illness his temperature began to drop and within twenty-four hours it dropped to 97 F. With this drop in temperature his pulse became rapid and thready, his color was ashen gray and his respirations were rapid and shallow. The blood pressure was 100 systolic and 88 diastolic. There was no pulmonary edema. There was no evidence of congestive heart failure. The heart sounds were of fair quality. I would appreciate the following information: 1. What is the probable mechanism of this reaction? 2. Are hemoconcentration, diminished circulating blood volume, capillary stasis and arteriolar spasm present? 3. What form of therapy is indicated to combat this emergency? 4. Are epinephrine, nikethamide and caffeine with sodium benzoate of value or are they contraindicated? 5. Are plasma, blood transfusion and parenteral fluids of value?

Captain, M. C., A. U. S.

ANSWER.—The type of alarming reaction described, for some unknown reason, seems to occur more commonly after the bacterial pneumonias which complicate influenza, as in the pandemic of 1918-1919, than after typical pneumococcic pneumonia. It also occurs after viral pneumonia, influenza, typhus and other acute infections. Its occasional occurrence during the crisis of pneumococcic pneumonia gave rise many years ago to the undue apprehension which still attends that phenomenon. It may occur at any time during the course of the disease.

The replies to the questions are as follows:

1. The mechanism of the reaction is poorly understood, but the condition is evidently related to shock or the shocklike state. Whether it is the result of a general "let down," asthenia or exhaustion after a severe disease or the exhaustion, failure or disturbance of a specific center or system such as the respiratory center (Cole, R. I., in Nelson's Loose Leaf Living Medicine **1**:203, 1920-1928. Reimann, H. A.: The Pneumonias, Philadelphia, W. B. Saunders Company, 1938, p. 59) or of vasomotor paralysis and failure of the circulatory system (Cecil, R. L.: *Arch. Int. Med.* **41**:295 [March] 1928. Perry, C. B.: *Quart. J. Med.* **3**:273 [April] 1934. Reimann: The Pneumonias, p. 68) is unknown. When it coincides with the crisis it may result from an inability of the particular system involved to readjust itself quickly to the suddenly changed condition arising between illness and recovery. Some (Warfield, L. M.: THE JOURNAL, March 14, 1936, p. 892) have ascribed the cause to "toxins" of the causative agents or to toxins resulting from their interaction with the tissues of the host. There is much to suggest a disturbance of the nervous system as an important factor. In the case described, signs of failure of the respiratory center seem to predominate over those of circulatory failure. See also Heffron, R.: Pneumonia, New York, Commonwealth Fund, 1939, page 545, for further discussion and references.

2. Hemoconcentration, diminished circulatory blood volume, capillary stasis and arteriolar spasm probably are present as in the other shocklike states, but the writer is unaware of any particular studies being made of the condition occurring specifically during the crisis of infectious disease.

3. The usual measures prescribed for the treatment of shock are indicated (see Warfield, *loc. cit.*).

4. The commonly used drugs mentioned have little or no value.

5. Parenteral injection of fluid, particularly of plasma, is usually advocated, but the problem of getting the fluid to move in the circulatory system seems to be of more importance than of simple replacement.

INTRAVENOUS ADMINISTRATION OF SALICYLATES —ACTION OF COLCHICINE

To the Editor:—Because of the local widespread use of intravenous sodium salicylate and the inconvenience caused both patient and doctor thereby, could you please tell me if the intravenous use has any advantage over the oral use in patients who tolerate the drug well by mouth? As a second question I should like to ask of what particular value in cases of arthritis, neuralgia, or myalgia, where gout is no factor, would the intravenous preparation of sodium salicylate 1 Gm. and sodium iodide 1 Gm. with colchicine 0.65 mg. have over the administration of these substances by mouth? As a third question, Has colchicine any rationale in the treatment of any other disease than true gout?

E. W. Saward, M.D., Hanford, Wash.

ANSWER.—Oral administration of the ordinary doses of sodium salicylate relieves the symptoms of rheumatic fever promptly and completely, unless vomiting sets in before a sufficient amount has been absorbed. If the drug is tolerated there would be no advantage in intravenous administration, and there would be the disadvantage of inconvenience and also some danger of colloidoclastic shock if the injection is made with ordinary speed, as shown by Hanzlik, De Eds and Tainter (*Arch. Int. Med.* **36**:447 [Oct.] 1925).

However, a new slant has been given to intravenous salicylate medication by A. F. Coburn (*Bull. Johns Hopkins Hosp.* **73**:435 [Dec.] 1943). He conceives the salicylate action as an interference with the inflammatory process which produces the cardiovascular injury, especially in the polycyclic recurrences of children and young adults. This antiphlogistic salicylate effect is reflected in the return of the blood sedimentation rate. It is perhaps explainable by the prevention of the precipitation of antigen by antibody, which has been demonstrated in the test tube. It is proportional to the salicylate level of the plasma. Coburn reports that plasma concentrations of 10 to 20 mg. per hundred cubic centimeters, which are obtained by the customary dosage and which relieve the symptoms satisfactorily, do not control the inflammatory process sufficiently to obviate the cardiovascular injury and that this requires plasma levels of at least 35 mg. per hundred cubic centimeters, which can be attained by daily administration of 10 Gm. of sodium salicylate. This may be done by oral administration, but it can be accomplished much more promptly by intravenous drip and, according to Coburn, with less nausea and other salicylism. He advises 10 Gm. of sodium salicylate in 1,000 cc. of 0.9 per cent sodium chloride solution by intravenous drip during four to six hours daily for six days (in severe cases, 20 Gm. in 1,000 cc. in eight hours); then 10 Gm. by mouth daily in divided doses for two weeks or more until a normal sedimentation rate has persisted for a week. This is very different from casual intravenous injections. It is a subject for controlled study, not for perfunctory routine use. Coburn's results are promising, but he concedes that the series is too small to discount the variable course of rheumatic fever.

Intravenous administration always involves some elements of risk and should be chosen only if the indications are clearcut, the advantages definite and the dangers minimal. Mixtures rarely fulfil these requirements; there is no therapeutic advantage in the intravenous injection of a salicylate-iodide-colchicine mixture, and it would be difficult to defend such practice in case of untoward reactions.

The action of colchicine in gout is unique and has not been adequately explained. It is effective only with doses that verge on the toxic. It has not been shown to be effective in other conditions, and such use is inadvisable especially in view of its toxicity.

FUNGOUS INFECTION OF NOSE

To the Editor:—A white man aged 30 has had a chronic vasomotor rhinitis for the past five years. Skin tests for possible allergy revealed a 3 plus reaction to dust and a 1 plus reaction to chocolate, rice, pear, cherry, cinnamon, grasses and ragweed. Allergic management failed to give relief. Following chemical cauterization seven months ago of the right inferior turbinate there was a severe aggravation of the symptoms. X-ray examinations of the sinuses were negative on three occasions, but clinically, during the winter, the patient has had sinusitis. Nasal smears on three occasions were negative for eosinophils but did reveal rather numerous yeast cells (2 to 3 per field). Cultures to identify the yeast organisms were unsuccessful on three occasions because of contamination with air borne molds. Owing to the character of the mucous secretion (thick, white, sticky) one is led to believe that this finding of yeast cells is of some significance. Will you kindly discuss the problem of nasal fungous infection and its management?

M.D., Illinois.

ANSWER.—Castellani says that "yeastlike and other fungi are often observed in the nasal mucus; they may play only a saprophytic role or they may give rise to an inflammation of the mucosa."

True yeast infection of the nasal mucosa and sinuses must be rare, in this country at least. Its occurrence is not mentioned in a single one of a dozen well known textbooks on rhinology.

All observers are agreed that the commonest pathogenic fungi to be seen in the nose belong to the Aspergillus family. Practically all observers are agreed also that the symptoms of fungous infection of the nose closely resemble those seen in allergic rhinitis. Especially are the bouts of sneezing emphasized.

The yeast cells described in the query, because they appeared after chemical cauterization of the nasal mucosa, may not be playing a pathogenic role but might be saprophytic in nature. Granting for sake of argument that they are truly disease causing, the treatment, which is far from being well defined, will vary, depending on whether the nasal mucosa alone or the accessory nasal sinuses (particularly the maxillary) are involved.

If the nasal mucosa alone is involved, iodine appears to be a favorite remedy. Lugol's solution may be given by mouth in increasing doses; so also may potassium or sodium iodide be given in the conventional amounts. There seems to be little said or done about the use of antiseptics or other medicaments locally in the nose.

When the disease is present in the sinuses (most often the maxillary) failure to respond to the usual irrigations should be, according to most authorities, good reason for removing the diseased mucosa operatively, preferably by way of a Caldwell-Luc procedure.